CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Human Immunodeficiency Virus – Apretude Utilization Management Medical Policy
- Apretude (cabotegravir intramuscular injection – ViiV)

REVIEW DATE: 01/14/2026

OVERVIEW

Apretude, a human immunodeficiency virus-1 (HIV-1) integrase strand transfer inhibitor (INSTI), is indicated for **pre-exposure prophylaxis (PrEP)** in at-risk adults and adolescents weighing ≥ 35 kg to reduce the risk of sexually acquired HIV-1 infection.[1]

Apretude is contraindicated in individuals with an unknown or positive HIV-1 status.[1] There is a risk of drug resistance with the use of Apretude for HIV-1 PrEP in undiagnosed HIV-1 Infection (Boxed Warning). Individuals must be tested for HIV-1 infection prior to initiating Apretude, (or Vocabria® [cabotegravir tablets]), and with each subsequent injection of Apretude, and as clinically appropriate using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of Apretude for HIV-1 PrEP by individuals with undiagnosed HIV-1 infection. If an antigen/antibody-specific test is used and provides negative results, then such negative results should be confirmed using an RNA-specific assay, even if the results of the RNA-assay are available after Apretude or Vocabria initiation. Do not initiate Apretude for HIV-1 PrEP unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving Apretude for PrEP must transition to a complete HIV-1 treatment regimen.

Apretude should also be used as part of a comprehensive prevention strategy including adherence to the administration schedule and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections.[1]

Dosing

Apretude is administered by intramuscular (IM) gluteal injections and must be given by a healthcare provider. Vocabria *may* be administered for approximately 1 month prior to Apretude (Table 1) or the patient may proceed directly to Apretude without an oral lead-in (Table 2). If an oral lead-in is used, Apretude should be administered on the last day of oral lead-in or within 3 days thereafter (Table 1). Note: Vocabria is only (and will only ever be) available from the manufacturer.

Dosing: The recommended initiation dose of Apretude is two, single 600 mg IM injections, given 1 month apart for 2 consecutive months (Months 1 and 2 if no oral lead-in is used [Months 2 and 3 if oral lead-in is used]).[1] After the initiation injection doses, the recommended continuation dose of Apretude is a single 600 mg IM injection every 2 months (Q2M) [starting at Month 4 if no oral-lead in is used or Month 5 if oral lead-in is used]. Apretude may be given up to 7 days before or after the date of the scheduled injection.

Table 1. Recommended Dosing Schedule (with Oral Lead-in) for PrEP.[1]

Oral Lead-in (at Least 28 Days)	IM (Gluteal) Initiation Injection (Month 2 and Month 3)	IM (Gluteal) Continuation Injection (Month 5 and Q2M Onwards)
Vocabria 30 mg QD for 28 days	Apretude 600 mg (3 mL)[a]	Apretude 600 mg (3 mL)[b]

PrEP – Pre-exposure prophylaxis; IM – Intramuscular; Q2M – Every 2 months; QD – Once daily; [a] Should be administered on the last day of oral lead-in or within 3 days thereafter; [b] Individuals may be given Apretude up to 7 days before or after the date the individual is scheduled to receive the injections.

Table 2. Recommended Dosing Schedule (Direct to Injection) for PrEP.[1]

IM (Gluteal) Initiation Injection (Month 1 and Month 2)	IM (Gluteal) Continuation Injection (Month 4 and Q2M Onwards)
Apretude 600 mg (3 mL)[a]	Apretude 600 mg (3 mL)[a]

PrEP – Pre-exposure prophylaxis; IM – Intramuscular; Q2M – Every 2 months; [a] Individuals may be given Apretude up to 7 days before or after the date the individual is scheduled to receive the injections.

Adherence to the injection dosing schedule is strongly recommended. Individuals who miss a scheduled injection visit should be clinically reassessed to ensure resumption of Apretude remains appropriate.

Planned Missed Injections: If an individual plans to miss a scheduled (Q2M) continuation injection visit by > 7 days, take Vocabria 30 mg once daily (QD) for a duration of up to 2 months to replace one missed scheduled (Q2M) injection. The first dose of Vocabria should be taken approximately 2 months after the last injection dose of Apretude. Restart Apretude on the day Vocabria dosing completes or within 3 days (Table 3). For Vocabria durations > 2 months, an alternative oral regimen is recommended.

Unplanned Missed Injections: If a scheduled injection visit is missed or delayed by > 7 days and oral dosing has not been taken in the interim, clinically reassess the individual to determine if resumption of Apretude remains appropriate (if the injection schedule will be continued, see Table 3).

Table 3. Apretude Dosing Recommendations After Missed Injections.[1]

Time Since Last Injection	Recommendation
Initiation Injection – If the second injection is missed and time since first injection is:	
≤ 2 months	Administer Apretude (600 mg) as soon as possible, then continue to follow the Q2M injection dosing schedule.
> 2 months	Restart Apretude (600 mg) with one injection, followed by a second injection (600 mg) 1 month later. Then, continue to follow the Q2M injection dosing schedule thereafter (starting at Month 4).
Maintenance Injection – If third or subsequent injection is missed and time since prior injection is:	
≤ 3 months	Administer Apretude as soon as possible, then continue with the Q2M injection dosing schedule.
> 3 months	Restart Apretude (600 mg) with one injection, followed by a second injection (600 mg) 1 month later. Then, continue to follow the Q2M injection dosing schedule thereafter (starting at Month 4).

Q2M – Every 2 months.

Dose modifications for Apretude are needed when administered with rifabutin. When rifabutin is started before or concomitantly with the first initiation injection of Apretude, the recommended dosing of Apretude is one 600 mg injection, followed 2 weeks later by a second 600 mg initiation injection and monthly thereafter while on rifabutin. When rifabutin is started at the time of the second initiation injection or later, the recommended dosing schedule of Apretude is 600 mg monthly while on rifabutin. After stopping rifabutin, the recommended dosing schedule of Apretude is 600 mg every 2 months.

Guidelines

Recommendations and guidelines for PrEP align with the Apretude prescribing information regarding the provision of a negative HIV-1 test prior to initiating PrEP and prior to each dose. Ideally, testing should be performed and results provided on the same day PrEP is offered; however, tests taken within 7 days of initiation of PrEP may be utilized.[3]

World Health Organization (WHO)

The WHO Guidelines on Lenacapavir for HIV Prevention and Testing Strategies for Long-Acting Injectable PrEP (2025) provide recommendations regarding testing in the setting of long-acting injectable PrEP, including Apretude.[2] The WHO also published an implementation tool for PrEP (2024) and Guidelines for Apretude for PrEP that similarly emphasizes the importance of HIV testing prior to starting

treatment and prior to each injection.[4,5] Ideally, HIV testing should be performed and results provided on the same day that PrEP is offered to facilitate same-day initiation of PrEP.[5] There is no evidence supporting the prioritization of antigen/antibody rapid diagnostic tests over antibody-only rapid diagnostic tests.[2] Only individuals who have an HIV-negative test result should be started on PrEP.[5] It is practical for individuals taking PrEP to receive testing at their refill or injection visit. Depending on the PrEP option used, HIV testing schedules may differ. For Apretude, following the two initiation injections/visits (Month 0 and Month 1), follow-up visits for continuation should be conducted every 2 months thereafter.[2,5] However, it is important to provide individuals with the flexibility to support effective PrEP use.[2] More, or less, frequent testing intervals may be considered where warranted and based on available resources. Self-tests can be a potential option where needed and considered beneficial by the individual or provider.

Individuals with a negative HIV test result should continue PrEP.[2] Anyone taking injectable PrEP who has a reactive HIV test result, including a self-test result, should receive further testing, to confirm an HIV diagnosis. Upon confirmation of a diagnosis, antiretroviral therapy should be initiated promptly. Individuals with an inconclusive HIV test status while taking injectable PrEP should be retested in 14 days to rule in or rule out seroconversion. If the serology profile remains inconclusive, the person receiving injectable is considered HIV-negative, and long-acting injectable PrEP can be continued. If the individual is diagnosed with HIV, they should be immediately referred for care and treatment.

Each suspected breakthrough infection should be evaluated individually.[2] Individuals should be encouraged to continue PrEP until more information and a final diagnosis are available, and they should consider taking precautions to prevent potential onwards transmission of HIV, such as the use of condoms during sex.

International Antiviral Society (IAS)-USA
The IAS-USA recommendations for the treatment and prevention of HIV note that any delay in starting PrEP in an individual likely to be exposed to HIV may be a missed opportunity to prevent HIV acquisition.[3] If negative HIV serologic test results are available from blood drawn within 7 days or a rapid (point-of-care) HIV antibody test result is negative on the day of PrEP initiation, PrEP initiation is recommended while awaiting additional diagnostics and safety assessment. For Apretude, HIV testing at initiation and at all visits should ideally include an HIV RNA test with a lower limit of quantification of ≤ 50 copies/mL AND a laboratory-based antigen-antibody test. If RNA testing is not available, Apretude can still be considered using rapid point-of-care HIV antibody screening while awaiting laboratory antigen-antibody test results. Follow-up testing for Apretude PrEP breakthrough infections should not routinely include HIV RNA testing but should include a point-of-care rapid HIV antibody test and a laboratory-based antigen/antibody test.

US Preventative Services Task Force (USPTF)
The USPTF recommendations for PrEP to prevent acquisition of HIV (2023) are similar to those discussed above.[6] All persons being considered for PrEP should have a recently documented negative HIV test. Prior to prescribing PrEP, clinicians should exclude individuals with acute or chronic HIV through medial history and HIV testing. Ongoing follow-up and monitoring, including HIV testing with the frequency determined by PrEP method, is recommended. Patients can continue PrEP for as long as the risk of acquisition continues. PrEP may be discontinued and re-initiated. Re-initiation should involve the same evaluation as initial therapy.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Apretude. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Apretude as well as the monitoring required for adverse events and long-term efficacy, approval requires Apretude to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Apretude is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Pre-exposure Prophylaxis (PrEP) of Human Immunodeficiency Virus-1 (HIV-1) Infection.** Approve for 5 months if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 35 kg; AND
   - **B)** According to the prescriber, the medication will be administered only if the patient has a negative HIV-1 test result ≤ 7 days prior to each dose of Apretude; AND
   - **C)** The medication is prescribed as part of a comprehensive HIV-1 prevention strategy (i.e., adherence to administration schedule and safer sex practices, including condoms); AND
   - **D)** The medication is prescribed by or in consultation with a physician who specializes in the management of HIV infection.

   Dosing. Approve ONE of the following dosing regimens (A or B):
   - **A)** Approve 600 mg intramuscularly for one dose, followed by 600 mg for a second dose 1 month ± 7 days later, then approve 600 mg intramuscularly once every 2 months ± 7 days thereafter.
   - **B)** If Apretude will be given concomitantly with rifabutin, approve Apretude 600 mg intramuscularly for one dose, followed by 600 mg for a second dose 2 weeks ± 7 days later, then approve 600 mg intramuscularly every 1 month ± 7 days thereafter.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Apretude is not recommended in the following situations:

1. **Treatment of Human Immunodeficiency Virus (HIV).** Apretude is not indicated for the treatment of HIV. It is inadequate therapy for established HIV infection and use in persons with early HIV infection may encourage resistance of one or more of the PrEP medications.[2]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Apretude® injectable suspension [prescribing information]. Research Triangle Park, NC: ViiV; April 2025.
2. Guidelines on lenacapavir for HIV prevention and testing strategies for long-acting injectable pre-exposure prophylaxis (PrEP). Geneva: World Health Organization; 2025. License: CC-BY-NC-SA 3.0 IGO
3. Ghandi RT, Landovitz RJ, Sax PE, et al. Antiretroviral drugs for treatment and prevention of HIV in adults: 2024 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2025;333(7):609-628.
4. Guidelines on long-acting injectable cabotegravir for HIV prevention. Geneva: World Health Organization; 2022. License: CC BY-NC-SA 3.0 IGO. Available at: https://www.who.int/publications/i/item/9789240054097. Accessed on January 16, 2025.
5. WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection: provider module for oral and long-acting PrEP. Geneva: World Health Organization; 2024. License: CC BY-NC-SA 3.0 IG.
6. US Preventative Services Task Force. Preexposure prophylaxis to prevent acquisition of HIV. US Preventative Tast Force Recommendation Statement. *JAMA*. 2023;330(8):736-745.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/24/2024
Selected Revision	**Pre-exposure Prophylaxis (PrEP) of Human Immunodeficiency Virus-1 (HIV-1) Infection.** The requirement that Apretude be prescribed by or in consultation with a physician who specializes in the treatment of HIV infection was changed to prescribed by or in consultation with a physician who specializes in the management of HIV infection.	06/05/2024
Annual Revision	No criteria changes.	01/29/2025
Selected Revision	**Pre-exposure Prophylaxis (PrEP) of Human Immunodeficiency Virus-1 (HIV-1) Infection.** The approval duration was changed to 5 months, previously it was 2 months. The criterion that required the medication be administered only if the patient has no signs or symptoms of acute HIV infection, according to the prescriber was removed. For the criterion "According to the prescriber, the medication will be administered only if the patient has a negative HIV-1 test result ≤ 7 days prior to each dose of Apretude", "according to the prescriber" was added. Additionally the timeframe was changed from ≤ 1 week to ≤ 7 days, and it was clarified that the negative test result is prior to "each" dose (previously was "the" dose). **Dosing.** The dosing was updated to include a grace period of ± 7 days throughout.	08/13/2025
Annual Revision	No criteria changes.	01/14/2026