Apretude (cabotegravir extended-release injectable suspension)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Pre-Exposure Prophylaxis (PrEP) is the use of anti-retroviral medications to prevent the acquisition of HIV. When taken consistently and correctly, PrEP can reduce the risk of HIV acquisition by over 99%. PrEP is not 100% effective and does not protect against other sexually transmitted infections (STIs). Therefore, condom use and frequent STI testing should be recommended PrEP is recommended for people who are at risk of acquiring HIV, particularly those who have multiple sexual partners, use injection drugs, have a partner with HIV, or engage in condomless sex. PrEP is also recommended for people who are HIV-negative and are planning to become pregnant with an HIV-positive partner. The need for PrEP should be patient-driven, and offered to all patients who could benefit from its use.

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians offer pre-exposure prophylaxis (PrEP) with effective antiretroviral therapy to individuals who are at high risk of HIV acquisition. This is a Grade A recommendation, indicating that the USPSTF believes there is a high certainty of substantial benefit from using PrEP in these populations.

- The specific drugs recommended for PrEP can vary based on the individual's health situation and the most current research.
- Historically, the combination of emtricitabine and tenofovir has been commonly used for PrEP.

Apretude (cabotegravir extended-release injectable suspension), for intramuscular use is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating Apretude (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

- Cabotegravir is a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI). It is available as oral tablets and an extended-release injection.
    - The oral tablets are approved for use in combination with rilpivirine for short-term treatment (as a lead-in to assess tolerability of cabotegravir before administering extended-release cabotegravir; rilpivirine injection or as a replacement for a missed injection) of HIV-1 infection in adults and children 12 years and older weighing at least 35 kg who are virologically suppressed on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.
    - The extended-release injection is approved for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and children 12 years and older who weigh at least 35 kg and are at high risk; it is the first injectable treatment for HIV-1 PrEP. The oral tablets may also be used short-term for PrEP as a lead-in to assess tolerability of cabotegravir before giving the extended-release injection or as a replacement for a missed injection. Cabotegravir injection may be especially appropriate for patients with significant renal disease, those who have had difficulty with adherent use of oral PrEP, and those who prefer injections every 2 months to an oral PrEP dosing schedule.
- The FDA-approved package labeling contains a Black Box Warning regarding risk of drug resistance with use of cabotegravir extended-release injection for PrEP in undiagnosed HIV-1 infection; individuals must be tested for HIV-infection prior to therapy initiation and with each subsequent injection.

Definitions

"**Human Immunodeficiency Virus (HIV)**" is a virus that attacks the immune system, leaving the body vulnerable to infections and diseases. It is primarily spread through sexual contact, sharing of needles or other injection equipment, or from mother to child during pregnancy, childbirth, or breastfeeding.

"**Antiretroviral Therapy (ART)**" is the treatment for HIV that involves taking a combination of medications that work to suppress the virus and prevent it from replicating in the body. ART is not a cure for HIV, but it can significantly reduce the amount of virus in the body, slow the progression of the disease, and improve the immune system's function.

"**Pre-Exposure Prophylaxis (PrEP)**" is the use of anti-retroviral medications to prevent the acquisition of HIV.

"**Acquired Immune Deficiency Syndrome (AIDS)**" is an outdated term that was previously used to describe advanced HIV disease and the loss immune function required to fight certain infections.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Apretude (cabotegravir)** medically necessary when **ALL** the following criteria are met:

1. The member is at least 12 years of age and weighing at least 35 kg (77 lbs) or greater; ***AND***
2. Is being prescribed for pre-exposure prophylaxis (PrEP) for members meeting **ONE** of the following criteria:
    a. to reduce the risk of sexually acquired HIV-1 (i.e., those with an HIV-positive sexual partner, recent sexually transmitted infection, multiple sex partners, history of inconsistent or no condom use, commercial sex work or transactional sex, in high-prevalence area or network); ***or***
    b. injection drug users at substantial risk of HIV acquisition (i.e., those with an HIV-positive injecting partner and those sharing injection equipment or who recently received drug treatment but are currently injecting); ***AND***
3. The member is documented to be HIV-1-negative; ***AND***
4. The member is unable to use, or has a documented clinical rationale indicating they are not an appropriate candidate (e.g., history of non-adherence to once-daily oral PrEP regimen, baseline renal dysfunction or at risk for developing renal impairment, osteoporosis, low bone mineral density, or at risk of developing low bone mineral density) for emtricitabine and tenofovir disoproxil fumarate (Truvada).

If the above prior authorization criteria is met, Apretude (cabotegravir) will be approved for 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if **BOTH** of the following are met:

1. the member still meets the applicable initial criteria***; AND***
2. recent chart documentation (within the last 3 months) shows the member has experienced therapeutic response to the requested medication as evidenced by a documented negative HIV test.

Experimental or Investigational / Not Medically Necessary

Apretude (cabotegravir) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
J0739	Injection, cabotegravir, 1 mg
CPT Modifier	
Code	*Description*
33	For delivery of an evidence-based service in accordance with a US Preventive Services Task Force A or B rating in effect and other preventive services mandated by legal or regulatory bodies.
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
Z01.812	Encounter for preprocedural laboratory examination
Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission

Z11.4	Encounter for screening for human immunodeficiency virus (HIV)
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission
Z20.5	Contact with and (suspected) exposure to viral hepatitis
Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus (HIV)
Z51.81	Encounter for therapeutic drug-level monitoring
Z72.51	High-risk heterosexual behavior
Z72.52	High-risk homosexual behavior
Z72.53	High-risk bisexual behavior
Z79.899	Other long-term (current) drug therapy

Appendix

Apretude (cabotegravir) provides an important new injectable option for PrEP that could increase adherence and decrease HIV acquisition risk compared to oral PrEP in appropriate candidates, including cisgender men and transgender women who have sex with men and women at high risk for HIV infection. However, oral PrEP remains appropriate for many patients based on individual preferences and other considerations.

- The injectable agent cabotegravir (Apretude) was FDA-approved based on two large trials (HPTN 083 and 084). In both trials, cabotegravir given intramuscularly every 2 months was superior to daily oral FTC/TDF in reducing HIV incidence.
    - In the HPTN 083 trial of cisgender men and transgender women who have sex with men, Apretude was superior to daily oral TDF-FTC for HIV prevention, with significantly lower rates of HIV acquisition (0.37 vs 1.22; HR 0.31 [95% CI 0.16-0.58]).
    - In the HPTN 084 trial of African women at high risk for HIV infection, Apretude was also superior to TDF-FTC, again with significantly lower HIV acquisition (0.15 vs 1.85; HR 0.10 [95% CI 0.03-0.27]).
    - Adherence to oral FTC/TDF based on drug levels was lower in these trials (74% and 46% of samples) compared to cabotegravir injections received per schedule (91% and 93%).

- Apretude offers the advantage of less frequent dosing and bypassing the need for daily oral adherence. This could promote adherence and increase PrEP effectiveness compared to daily oral TDF-FTC.
    - Two once-daily oral antiretroviral regimens are FDA-approved for PrEP: emtricitabine/tenofovir disoproxil fumarate (FTC/TDF; Truvada) and emtricitabine/tenofovir alafenamide (FTC/TAF; Descovy).
    - FTC/TDF can be used in any PrEP-eligible patient, while FTC/TAF is not indicated for females at risk from receptive vaginal intercourse.
    - Both regimens significantly reduce the risk of HIV infection when taken daily, but adherence is critical to maximize efficacy. They are not recommended in severe renal impairment (i.e., creatinine clearance <30 mL/min).
- Apretude offers less frequent dosing and may increase adherence compared to daily oral PrEP, but requires regular injections and has risks like injection site reactions.

References

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Clinical Guideline Revision / History Information

Original Date: 9/05/2023 Reviewed/Revised: