Clinical Policy: Cabotegravir (Apretude), Cabotegravir/Rilpivirine (Cabenuva)

Reference Number: MDN.CP.PHAR.573
Effective Date: 04.01.22
Last Review Date: 04.22
Line of Business: Illinois Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Cabotegravir (Apretude™) is a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI). Cabotegravir/rilpivirine (Cabenuva®) is a 2-drug co-packaged product of cabotegravir and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI).

FDA Approved Indication(s)

Apretude 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.

Cabenuva is indicated for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 ribonucleic acid (RNA) less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Apretude and Cabenuva are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Human Immunodeficiency Virus Type-1 Infection (must meet all)**:**

1. Request is for Cabenuva;
2. Diagnosis of HIV-1 infection;
3. Age ≥ 18 years;
4. Documentation of adherence to a stable oral antiretroviral regimen for HIV-1 for ≥ 3 months;
5. Documentation of sustained virologic suppression as evidenced by HIV RNA viral load < 50 copies/mL for ≥ 3 months;
6. Member has no history of treatment failure (*see Appendix D*);
7. Member has no known or suspected resistance to either cabotegravir or rilpivirine;

8. Member will be initiated on oral Vocabria® and Edurant® for ≥ 28 days prior to initiation of Cabenuva to assess for tolerability;
9. Dose does not exceed (a or b):
   a. Monthly schedule: 600 mg cabotegravir and 900 mg rilpivirine (1 kit of 2 vials) initiation dose,* followed by 400 mg cabotegravir and 600 mg rilpivirine (1 kit of 2 vials) every month thereafter;
   **An initiation dose may be repeated if member misses more than 2 monthly scheduled continuation injections*
   b. Every 2-month schedule: 600 mg cabotegravir and 900 mg rilpivirine (1 kit of 2 vials) 1 month apart for 2 consecutive months (initial dose), followed by 600 mg cabotegravir and 900 mg rilpivirine (1 kit of 2 vials) every 2 months thereafter.

Approval duration: Indefinite

B. Pre-exposure HIV Prophylaxis (must meet all)**:**
1. Request is for Apretude;
2. Member is HIV-negative has no signs or symptoms of acute HIV infection;
3. Member is considered at high risk for acquiring HIV and meets one of the following (a, b, or c):
   a. Engaging in sexual activity with an HIV-1 infected partner;
   b. Engaging in sexual activity and one or more of the following:
      i. Inconsistent or no condom use;
      ii. Diagnosis of sexually transmitted infections in the past 6 months;
      iii. Exchange of sex for commodities;
      iv. Incarceration;
      v. Not in a monogamous partnership;
      vi. Partner of unknown HIV status with any of the preceding risk factors;
   c. Use of illicit injection drugs;
4. Member weighs ≥ 35 kg;
5. Member must instead use emtricitabine/tenofovir disoproxil fumarate (generic Truvada), unless contraindicated, clinically significant adverse effects are experienced, or member has bone/renal co-morbidities or risk factors (*see Appendix E*);
6. Dose does not exceed a 600 mg intramuscular injection given 1 month apart for 2 consecutive months (initial dose), followed by single 600 mg intramuscular injection given every 2 months thereafter.

Approval duration: 12 months (7 injections)

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Human Immunodeficiency Virus Type-1 Infection (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Cabenuva for a covered indication and has received this medication for at least 30 days;

2. Request is for Cabenuva;
3. If request is for a dose increase, new dose does not exceed (a, b, or c):
   a. 400 mg cabotegravir and 600 mg rilpivirine (1 kit of 2 vials) every month;
   b. 600 mg cabotegravir and 900 mg rilpivirine (1 kit of 2 vials) every 2 months;
   c. If member has missed injections (≥ 2 injections if on monthly schedule or just one injection if on every 2-month schedule) as evidenced by claims history, both of the following (i and ii):
      i. Provider attestation that member remains an appropriate candidate for therapy;
      ii. Follow recommended dosing schedule for missed injections (*see Appendix F*).

Approval duration: Indefinite

B. Pre-exposure HIV Prophylaxis (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Apretude for a covered indication and has received this medication for at least 30 days;
2. Request is for Apretude;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed a single 600 mg intramuscular injection given every 2 months.

Approval duration: 12 months (6 injections)

C. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HBV: hepatitis B virus
HIV-1: human immunodeficiency virus type 1
INSTI: integrase strand transfer inhibitor
NNRTI: non-nucleoside reverse transcriptase inhibitor
NRTI: nucleos(t)ide reverse transcriptase inhibitor
PI: protease inhibitor
PrEP: pre-exposure prophylaxis
RNA: ribonucleic acid

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Nucleos(t)ide reverse transcriptase inhibitors (NRTIs) (e.g., abacavir, tenofovir disoproxil fumarate, Emtriva®)	Refer to prescribing information	Refer to prescribing information
Non-nucleoside reverse transcriptase inhibitors (NNRTIs) (e.g., efavirenz, nevirapine, Edurant®)	Refer to prescribing information	Refer to prescribing information
Protease inhibitors (PIs) (e.g., atazanavir, fosamprenavir, Invirase®, Viracept®)	Refer to prescribing information	Refer to prescribing information
Integrase inhibitors (INSTIs) (e.g., Isentress®, Vocabria®)	Refer to prescribing information	Refer to prescribing information
Fuzeon® (enfurvirtide)	Refer to prescribing information	Adults: 180 mg/day Children 6 years and older: 4 mg/kg/day
Selzentry® (maraviroc)	Refer to prescribing information	600 mg/day; 1,200 mg/day if taking a potent CYP3A inducer
Fixed-dose combinations (e.g., Genvoya®, Stribild®, Odefsey®, Descovy®, Truvada®)	Refer to prescribing information	Refer to prescribing information
emtricitabine and tenofovir disoproxil fumarate (Truvada)	**PrEP:** One tablet (200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate) PO QD	Refer to prescribing information

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Apretude: unknown or positive HIV-1 status, previous hypersensitivity reaction to cabotegravir
  - Cabenuva: previous hypersensitivity to Cabenuva or any of its components, coadministration with uridine diphosphate (UDP)-glucuronosyl transferase (UGT)1A1 and/or cytochrome P450(CYP)3A4 enzyme induction drugs for which significant decreases in cabotegravir and/or rilpivirine plasma concentrations may occur, which may result in loss of virologic response
- Boxed warning(s):

- Apretude: risk of drug resistance with use of Apretude for HIV-1 PrEP in undiagnosed HIV-1 infection
- Cabenuva: none reported

Appendix D: General Information
Per the Department of Health and Human Services Antiretroviral Guidelines:

- Evaluation of virologic failure should include assessment of adherence, drug-drug and drug-food interactions, drug tolerability, HIV RNA, and CD4 T lymphocyte cell count trends over time, treatment history, and prior and current drug-resistance testing results.
- Virologic failure is defined as the inability to achieve or maintain suppression of viral replication to HIV RNA level < 200 copies/mL. Patients with levels persistently above 200 copies/mL, especially > 500 copies/mL, often develop drug resistance.
- Cabenuva can be used after oral lead-in therapy to replace an existing oral antiviral regimen in people with HIV with sustained viral suppression for 3 to 6 months, no baseline resistance to either medication and no prior virologic failures (AI recommendation).

Appendix E: Examples of Bone/Renal Co-morbidities and Risk Factors
Examples include, but are not limited to:

- Bone disease: osteoporosis, osteopenia, receiving chronic corticosteroids or other therapies known to decrease bone density (e.g., aromatase inhibitors, androgen deprivation therapy, doxorubicin, cyclophosphamide), frail/underweight
- Renal disease: chronic kidney disease, estimated creatinine clearance < 60 mL/min, albuminuria, family history of kidney disease, diabetes, receiving nephrotoxic medications

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Apretude	HIV-1 PrEP	*Initiation* A single 600 mg IM gluteal injection given 1 month apart for 2 consecutive months (on the last day of an oral lead-in if used or within 3 days) *Continuation* 600 mg IM gluteal injection every 2 months	600 mg every 2 months
Cabenuva	HIV-1 infection	Lead-in with oral cabotegravir 30 mg and rilpivirine 25 mg daily with meals for 1 month (28 days) Monthly Dosing Schedule Initiate with 600 mg cabotegravir and 900 mg rilpivirine IM on the last day of oral lead-in and continue with IM injections of 400 mg cabotegravir and 600 mg rilpivirine every month thereafter.	400 mg cabotegravir and 600 mg rilpivirine every month OR 600 mg cabotegravir and

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Every 2 Month Dosing Schedule Initiate injection on the last day of oral lead in. Initiate with 600 mg cabotegravir and 900 mg rilpivirine IM 1 month apart for 2 consecutive months. After 2 initiation doses given consecutively, then continue with IM injections of 600 mg cabotegravir and 900 mg rilpivirine every 2 months thereafter.	900 mg rilpivirine every 2 months

VI. Product Availability

Drug	Availability
Apretude	Single-dose vial: 600 mg/3 mL (200 mg/mL)
Cabenuva	Injectable suspension kits: • Cabenuva 400 mg/600 mg kit: cabotegravir 400 mg/2 mL (200 mg/mL) vial / rilpivirine 600 mg/2mL (300 mg/mL) vial • Cabenuva 600 mg/900 mg kit: cabotegravir 600 mg/3 mL (200 mg/mL) vial / rilpivirine 900 mg/3mL (300 mg/mL) vial

VII. References

1. Apretude Prescribing Information. Research Triangle Park, NC: ViiV Healthcare; December 2021. Available at: www.apretude.com. Accessed January 11, 2022.
2. Cabenuva Prescribing Information. Research Triangle Park, NC: GlaxoSmithKine; January 2022. Available at: www.cabenuva.com. Accessed February 2, 2022.
3. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/. Last updated August 16, 2021. Accessed January 4, 2022.
4. Centers for Disease Control and Prevention, U.S. Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States - 2021 update. 2021. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Accessed January 11, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0741	Injection, cabotegravir and rilpivirine, 2 mg/3mg
C9399, J3490	Injection, cabotegravir extended-release

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created, adapted from CP.PHAR.573 to meet HFS requirements	3.18.22	04.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.