cabotegravir intramuscular injection (Apretude®)

Policy # 00828
Original Effective Date: 02/13/2023
Current Effective Date: 02/13/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider cabotegravir extended-release injectable suspension (Apretude®)‡ for pre-exposure prophylaxis (PrEP) of Human Immunodeficiency Virus-1 (HIV-1) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for cabotegravir extended-release injectable suspension (Apretude) will be considered when the following criteria are met:

- Patient is requesting Apretude for pre-exposure prophylaxis (PrEP) of HIV-1; AND
- Patient has a negative HIV-1 test prior to beginning therapy with Apretude; AND
- Patient weighs at least 35 kg; AND
- Patient is an adult or adolescent 12 years of age or older; AND
- Patient is "at risk" of sexually acquiring HIV-1 infection; AND
  (Note: Risk of HIV-1 acquisition includes behavioral, biological, or epidemiologic factors including, but not limited to, condomless sex, past or current sexually transmitted infections, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high prevalence area or network.)
- Requested dose is equal to 600 mg given 1 month apart for 2 consecutive months followed by 600 mg given every 2 months thereafter.

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers cabotegravir extended-release injectable suspension (Apretude) for any non-FDA approved indication to be **investigational.***

Based on review of available data, the Company considers the use of cabotegravir extended-release injectable suspension (Apretude) when the patient selection criteria are not met to be **investigational.***

Background/Overview

Apretude is indicated in at risk adults and adolescents weighing at least 35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection. It is available as a single dose vial consisting of 600 mg/3 ml of cabotegravir extended release in an injectable suspension formulation. Apretude is to be initiated with a single injection given 1 month apart for 2 consecutive months and then every 2 months thereafter. Providers have the option of using an oral lead in prior to administering Apretude injections to assess tolerability of cabotegravir, also. The oral lead in consists of administering oral cabotegravir 30 mg by mouth once daily for 28 days. If an oral lead in is used, Apretude injection should be administered on the last day of the oral lead in or within three days of the last oral dose. All patients should be screened for HIV-1 infection immediately prior to initiating Apretude and prior to each injection while taking Apretude. Adherence to the Apretude injection schedule is strongly recommended; however, information on how to proceed in the event of a missed dose can be found in the package insert.

Apretude is the first long-acting therapy for PrEP. It has already been integrated into clinical practice guidelines along with the two other agents currently approved for PrEP, Truvada and Descovy. Truvada is recommended for all populations at risk of HIV acquisition. In addition, it is also recommended for at-risk individuals who are pregnant or breastfeeding. Although it is FDA approved in at risk individuals excluding those at risk from receptive vaginal sex, Descovy is recommended in the subset of men who have sex with men (MSM) with a creatinine clearance (CrCl) $\geq$ 30 mL/min and < 60 mL/min who have a history of osteopenia or osteoporosis, or who are at high-risk for these complications. Unlike Truvada and Descovy, Apretude does not have renal dose

adjustment considerations. Truvada and Descovy are both dosed daily, and Truvada has a generic equivalent that is available. HIV-1 testing is recommended every 3 months while taking daily oral PrEP and prior to each injection with Apretude which is every 2 months. Apretude should be considered in patients with significant renal disease, those who have difficulty with adherence to daily oral PrEP, and those who prefer injections every 2 months to a daily oral PrEP dosing schedule.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Apretude is an HIV-1 integrase strand transfer inhibitor (INSTI) that was approved in December of 2021 and is indicated in at risk adults and adolescents weighing at least 35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Apretude to reduce the risk of acquiring HIV-1 infection were evaluated in 2 randomized, double-blind, controlled, multinational trials, Trial 1 in HIV-1 uninfected men and transgender women who have sex with men and have evidence of high-risk behavior for HIV-1 infection and Trial 2 in HIV-1 uninfected cisgender women at risk of acquiring HIV-1.

Participants randomized to receive Apretude initiated oral lead-in dosing with 1 oral cabotegravir 30-mg tablet and a placebo daily for up to 5 weeks, followed by Apretude 600-mg (3-mL) intramuscular injection at months 1 and 2 and every 2 months thereafter and a daily placebo tablet. Participants randomized to receive Truvada initiated oral Truvada (TDF 300 mg/FTC 200 mg) and placebo daily for up to 5 weeks, followed by oral Truvada daily and placebo intramuscular injection at months 1 and 2 and every 2 months thereafter.

Trial 1
In Trial 1, a non-inferiority study, 4,566 cisgender men and transgender women who have sex with men were randomized 1:1 and received either Apretude or Truvada as blinded study medication up to Week 153. The study included three phases, an oral-tablet lead-in phase, an injection phase, and a "tail phase", the time beginning 8 weeks after the final injection and continuing for approximately 48 weeks. During the lead-in phase, all patients received two oral tablets (one active and one placebo) daily for 5 weeks. Oral cabotegravir 30 mg was given daily for patients assigned to receive Apretude and active Truvada was given for patients assigned to receive Truvada. The primary endpoint was the rate of incident HIV-1 infections among participants randomized to daily oral cabotegravir and intramuscular injections of Apretude every 2 months compared with daily oral Truvada (corrected for early stopping). The primary analysis demonstrated the superiority of Apretude compared with Truvada with a 66% reduction in the risk of acquiring HIV-1 infection, hazard ratio (95% CI) 0.34 (0.18, 0.62); further testing revealed 1 of the infections on Apretude to be prevalent then yielding a 69% reduction in the risk of HIV-1 incident infection relative to Truvada. Among the 52 HIV-1 infections in total, 13 were reported in the Apretude group (incidence 0.41/100 person-years) and 39 were reported in the Truvada group.

Trial 2
Trial 2 was a Phase III, double-blind, double-dummy, multicenter (Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, and Zimbabwe), superiority trial that randomized 3,224 cisgender women to Apretude or Truvada for up to 153 weeks.

Patients were randomized to Group A (Apretude) or Group B (Truvada) that included three steps: Step 1 consisted of approximately 1 month of oral cabotegravir 30 mg daily (and placebo tablets daily) or Truvada daily (and placebo tablets daily); Step 2 consisted of up to 153 weeks of Apretude 600 mg IM every 2 months (and placebo tablets daily) or Truvada tablets daily (and placebo IM every 2 months); and Step 3 consisted of open-label Truvada daily for approximately 1 year after patients completed their last injection.

The primary endpoint was the rate of incident HIV-1 infections among participants randomized to oral cabotegravir and injections of Apretude compared with oral Truvada (corrected for early stopping). The primary analysis demonstrated the superiority of Apretude compared with Truvada with an 88% reduction in the risk of acquiring incident HIV-1 infection, hazard ratio (95% CI) 0.12 (0.05, 0.31); further testing revealed 1 of the infections on Apretude to be prevalent then yielding a

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90% reduction in the risk of HIV-1 incident infection relative to Truvada. Among the 39 HIV-1 infections reported after enrollment, 3 were in the Apretude group and 36 were noted in the Truvada group.

References

1. Apretude [package insert]. ViiV Healthcare. Research Triangle Park, North Carolina. Updated December 2021.
2. Apretude. Drug Evaluation. Express Scripts. January 2022.

Policy History

Original Effective Date: 02/13/2023
Current Effective Date: 02/13/2023
01/05/2023 Medical Policy Committee review
01/11/2023 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 01/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy

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Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No code
HCPCS	J0739
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment,

would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.