Long-Acting Injectable Antiretroviral Agents for HIV

Policy Number: IEXD0103.16
Effective Date: November 1, 2025

Ü Instructions for Use

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Related Policy

- Review at Launch for New to Market Medications

Applicable States

This Medical Benefit Drug Policy applies to Individual Exchange benefit plans in all states except for Massachusetts, Nevada, and New York.

Coverage Rationale

Ü See Benefit Considerations

This policy refers to the following long-acting injectable antiretroviral products:

- Apretude (cabotegravir)
- Cabenuva (cabotegravir/rilpivirine)
- Sunlenca (lenacapavir)
- Yeztugo (lenacapavir)

This policy refers to Sunlenca injection and Yeztugo injection for administration by a healthcare professional. Sunlenca oral tablets and Yeztugo oral tablets are obtained under the pharmacy benefit.

Apretude

Apretude (cabotegravir) is proven and medically necessary to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents weighing at least 35kg when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Used for HIV-1 pre-exposure prophylaxis (PrEP); **and**
  - Patient has a negative HIV-1 test; **and**
  - Provider confirms that the patient will be tested for HIV-1 infection with each subsequent injection; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization is for no more than 12 months
- For **continuation therapy**, **all** of the following:
  - Patient has previously received treatment with Apretude; **and**
  - Patient has a negative HIV-1 test; **and**
  - Provider confirms that the patient will be tested for HIV-1 infection with each subsequent injection; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months

Apretude is unproven and not medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1).

Cabenuva

Cabenuva (cabotegravir/rilpivirine) is proven and medically necessary for the treatment of a human immunodeficiency virus type-1 (HIV-1) in patients who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of HIV-1 infection; **and**
  - Patient has no prior virologic failures or baseline resistance to either cabotegravir or rilpivirine; **and**
  - Patient is currently on a stable antiretroviral regimen; **and**
  - Provider attests that patient has achieved viral suppression (HIV-1 RNA less than 50 copies per mL) for at least 3 months prior to initiation of Cabenuva; **and**
  - Provider attests that patient demonstrates treatment readiness by **both** of the following:
    - Patient understands the risks of missed doses of Cabenuva; **and**
    - Patient has the ability to adhere to the required monthly or every 2 months injection appointments **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization is for no more than 12 months
- For **continuation therapy**, **all** of the following:
  - Patient has previously received treatment with Cabenuva; **and**
  - Provider confirms that the patient has achieved and maintained viral suppression (HIV-1 RNA less than 50 copies per mL) while on Cabenuva therapy; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months

Cabenuva is unproven and not medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1) in patients who are not currently virally suppressed (HIV-1 RNA less than 50 copies per mL).

Sunlenca

Sunlenca (lenacapavir) is proven and medically necessary for the treatment of multi-drug resistant human immunodeficiency virus (HIV) in patients who meet all of the following criteria:

- For **initial therapy**, **all** of the following:
  - **Both** of the following:
    - Diagnosis of HIV-1 infection; **and**
    - Provider attestation that the patient has multi-drug resistant HIV-1 infection **and**
  - Provider confirms that the patient has been prescribed an optimized background antiretroviral regimen, containing at least one antiretroviral agent that demonstrates full viral sensitivity/susceptibility; **and**
  - Sunlenca initial and maintenance dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization is for no more than 12 months
- For **continuation therapy**, **all** of the following:
  - Patient has previously received treatment with Sunlenca; **and**
  - Provider confirms that the patient has achieved a clinically significant viral response to Sunlenca therapy; **and**
  - Provider confirms that the patient will continue to take an optimized background antiretroviral regimen, in combination with Sunlenca; **and**
  - Sunlenca maintenance dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months

Sunlenca is unproven and not medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1) in patients who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) for the treatment of HIV-1, in antiretroviral (ARV) naïve patients, and for HIV-1 pre-exposure prophylaxis (PrEP).

Yeztugo (Lenacapavir)

Yeztugo (lenacapavir) is proven to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents weighing at least 35kg. Yeztugo is medically necessary when the following additional criteria are met:

- For **initial therapy**, **all** of the following:
  - Used for HIV-1 pre-exposure prophylaxis (PrEP); **and**
  - Patient has a negative HIV-1 test; **and**
  - Provider confirms that the patient will be tested for HIV-1 infection with each subsequent injection; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization is for no more than 12 months
- For **continuation therapy**, **all** of the following:
  - Patient has previously received treatment with Yeztugo; **and**
  - Patient has a negative HIV-1 test; **and**
  - Provider confirms that the patient will be tested for HIV-1 infection with each subsequent injection; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months

Yeztugo is unproven and not medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0738	Injection, lenacapavir, 1 mg, FDA approved prescription, only for use as HIV pre-exposure prophylaxis (not for use as treatment for HIV)
J0739	Injection, cabotegravir, 1 mg, FDA-approved prescription, only for use as HIV pre-exposure prophylaxis (not for use as treatment for HIV)
J0741	Injection, cabotegravir and rilpivirine, 2mg/3mg
J1961	Injection, lenacapavir (only for use as HIV treatment), 1 mg

Diagnosis Code	Description
B20	Human immunodeficiency virus (HIV) disease
Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission
Z11.4	Encounter for screening for human immunodeficiency virus (HIV)
Z16.33	Resistance to antiviral drug(s)
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission
Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus (HIV)
Z21	Asymptomatic human immunodeficiency virus (HIV) infection status
Z29.81	Encounter for HIV pre-exposure prophylaxis
Z72.51	High risk heterosexual behavior
Z72.52	High risk homosexual behavior
Z72.53	High risk bisexual behavior

Background

Apretude (cabotegravir) inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration which is essential for the HIV replication cycle. Blocking this key function within the HIV replication cycle plays a role in both treatment and prevention.

Cabenuva (cabotegravir/rilpivirine) is a two-drug co-packaged product of extended-release injectable suspension formulations of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI),

and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI). Cabotegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration which is essential for the HIV replication cycle. Rilpivirine is a diarylpyrimidine NNRTI of HIV-1 and inhibits HIV-1 replication by non-competitive inhibition of HIV-1 reverse transcriptase (RT).

Lenacapavir, available as brand **Sunlenca** and brand **Yeztugo** is a multistage, selective inhibitor of HIV-1 capsid function that directly binds to the interface between capsid protein (p24) subunits in hexamers. Surface plasmon resonance sensorgrams showed dose-dependent and saturable binding of lenacapavir to cross-linked wild-type capsid hexamer with an equilibrium binding constant (KD) of 1.4 nM. Lenacapavir inhibits HIV-1 replication by interfering with multiple essential steps of the viral lifecycle, including capsid-mediated nuclear uptake of HIV-1 proviral DNA (by blocking nuclear import proteins binding to capsid), virus assembly and release (by interfering with Gag/Gag-Pol functioning, reducing production of capsid protein subunits), and capsid core formation (by disrupting the rate of capsid subunit association, leading to malformed capsids).

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

The efficacy of Apretude has been evaluated in two randomized, double-blind, controlled, multinational trials:

- Trial 201738 [HPTN 083 (NCT02720094)], (n = 4,566): HPTN 083 was a non-inferiority study in cisgender men and transgender women who have sex with men who were randomized 1:1 and received either Apretude (n = 2,281) or Truvada (n = 2,285) as a blinded study up to Week 153. At baseline, the median age of participants was 26 years, 12% were transgender women, 72% were non-White, and 67% were younger than 30 years. 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.
- Trial 201739 [HPTN 084 (NCT03164564)], (n = 3,224): HPTN 084 was a superiority study in cisgender women who were randomized 1:1 and received either Apretude (n = 1,614) or Truvada (n = 1,610) as blinded study medication up to Week 153. At baseline, the median age of participants was 25 years, > 99% were non-White, > 99% were cisgender women, and 49% were < 25 years of age. 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 90% reduction in the risk of HIV-1 incident infection relative to Truvada.

In December 2021, the Centers for Disease Control and Prevention published the US Public Health Service Pre-Exposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update – A Clinical Practice Guideline.[6] The updated included a new section about prescribing PrEP with intramuscular injections of cabotegravir in anticipation of likely FDA approval in early 2022. A recommendation was added that states PrEP with intramuscular cabotegravir injections (conditional on FDA approval) is recommended for HIV prevention in adults reporting sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition. Regarding prescribing cabotegravir PrEP injections, the following information is included: “Patients considering PrEP should be informed of all FDA approved options. Cabotegravir injections 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 efficacy of Cabenuva has been evaluated in three Phase 3 randomized, multicenter, active controlled, parallel-arm, open-label, non-inferiority trials:

- Trial 201584 [FLAIR, (NCT02938520)], (n = 629): HIV-1–infected, antiretroviral treatment (ART) – naive subjects received a dolutegravir INSTI-containing regimen for 20 weeks (either dolutegravir/abacavir/lamivudine or dolutegravir plus two other NRTIs if subjects were HLA-B*5701 positive). Subjects who were virologically suppressed (HIV-1 RNA less than 50 copies/mL, n = 566) were then randomized (1:1) to receive either a cabotegravir plus rilpivirine regimen or remain on the current antiretroviral regimen. Subjects randomized to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg Vocabria (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least four weeks followed by monthly injections with Cabenuva for an additional 44 weeks.
- Trial 201585 [ATLAS, (NCT02951052)], (n = 616): HIV-1–infected, ART-experienced, virologically-suppressed (for at least six months; median prior treatment duration was 4.3 years) subjects (HIV-1 RNA less than 50 copies/mL) were randomized and received either a cabotegravir plus rilpivirine regimen or remained on their current antiretroviral regimen. Subjects randomized to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg Vocabria (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least four weeks followed by monthly injections with Cabenuva for an additional 44 weeks.
- Trial 207966 [ATLAS-2M, (NCT03299049)], (n = 1,045): HIV-1–infected, ART-experienced, virologically suppressed subjects, including 504 subjects from the ATLAS trial [randomized to CAB plus RPV (n = 253) or CAR (n = 251); prior exposure to cabotegravir plus rilpivirine (n = 391)], were randomized and received a cabotegravir plus rilpivirine regimen administered as injection doses of cabotegravir 400 mg plus rilpivirine 600 mg either monthly or cabotegravir 600 mg plus rilpivirine 900 mg every 2 months. Subjects without prior exposure to cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg VOCABRIA (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least 4 weeks followed by monthly or every-2-month injections with Cabenuva for an additional 44 weeks. The primary endpoint of ATLAS-2M was the proportion of subjects with a plasma HIV-1 RNA ^{3} 50 copies/mL at Week 48. The primary endpoint was met with 2% of subjects in the every 2-month dosing arm having an HIV-RNA ≥ 50 copies/mL compared to 1% in the monthly dosing arm.

The primary analysis was conducted after all subjects completed their week 48 visit or discontinued the trial prematurely. The primary endpoint of FLAIR and ATLAS was the proportion of subjects with plasma HIV-1 RNA greater than or equal to 50 copies/mL at week 48. In both FLAIR and ATLAS 2% of subjects met the primary endpoint as compared to 2% and 1% in the comparator arms respectively. Subjects in both the FLAIR and ATLAS trials were virologically suppressed prior to Day 1 or at study entry, respectively, and no clinically relevant change from baseline in $CD4^{+}$ cell counts was observed.

The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) updated the *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV* in September 2024. In these guidelines, it is recommended that monthly or every 2-month Cabenuva can be used to replace an existing oral ARV regimen in people with HIV who fulfill all of the following criteria:

- Sustained viral suppression for at least 3 months
- No history of documented or suspected resistance to either CAB or RPV
- No active HBV infection (unless also receiving TAF, TDF, or entecavir)
- Not pregnant or actively planning pregnancy
- Not receiving medications with significant drug interactions with oral (during lead-in or bridging therapy) or injectable CAB or RPV

Oral lead-in therapy with CAB and RPV is optional and can be done based on provider–patient discussion.

For patients with multidrug resistance and ongoing detectable viremia without sufficient treatment options to construct a fully suppressive regimen, the Panel recommends that they may be candidates for Trogarzo (ibalizumab), Rukobia (fostemsavir), and/or Sunlenca (lenacapavir).

The efficacy of Sunlenca in HIV-1 infected, heavily treatment-experienced subjects with multidrug resistance has been evaluated in a 52-week, randomized, placebo-controlled, double-blind, multicenter Phase 2/3 study (CAPELLA; NCT 04150068). CAPELLA was conducted in 72 heavily treatment-experienced subjects with multiclass resistant HIV-1. Subjects were required to have a viral load ≥ 400 copies/mL, documented resistance to at least two antiretroviral medications from each of at least 3 of the 4 classes of antiretroviral medications (NRTI, NNRTI, PI and INSTI), and ≤ 2 fully active antiretroviral medications from the 4 classes of antiretroviral medications remaining at baseline due to resistance, intolerability, drug access, contraindication, or other safety concerns. The trial was composed of two cohorts. Subjects were enrolled into the randomized cohort (cohort 1, n = 36) if they had a < 0.5 $\log_{10}$ HIV-1 RNA decline compared to the screening visit. Subjects were enrolled into the non-randomized cohort (cohort 2, n = 36) if they had a ≥ 0.5 $\log_{10}$ HIV-1 RNA decline compared to the screening visit or after cohort 1 reached its planned sample size. In the 14-day functional monotherapy period, subjects in cohort 1 were randomized in a 2:1 ratio in a blinded fashion to receive either Sunlenca or placebo, while continuing their failing regimen. This period was to establish the virologic activity of Sunlenca. After the functional monotherapy period, subjects who had received Sunleca continued on Sunlenca along with

an optimized background regimen (OBR); subjects who had received placebo during this period initiated Sunlenca along with an OBR. Subjects in cohort 2 initiated SUNLENCA and an OBR on Day 1. The primary efficacy endpoint was the proportion of subjects in cohort 1 achieving ≥ 0.5 log_{10} copies/mL reduction from baseline in HIV-1 RNA at the end of the functional monotherapy period. The proportion of subjects achieving a ≥ 0.5 log_{10} decrease in viral load was 87.5% in the Sunlenca group vs. 16.7% in the placebo group (treatment difference 70.8%; 95% CI: 34.9, 90.0; p < 0.0001). In cohort 1, at Weeks 26 and 52, the mean change from baseline in $CD4^+$ cell count was 81 cells/mm^3 (range: -101 to 522) and 82 cells/mm^3 (range: -194 to 467), respectively. In cohort 2, at Week 26 and 52, 81% (29/36) and 72% (26/36) of patients achieved HIV1 RNA < 50 copies/mL, respectively, and the mean change from baseline in $CD4^+$ cell count was 97 cells/mm^3 (range: -103 to 459) and 113 cells/mm^3 (range: -124 to 405), respectively.

The efficacy of Yeztugo was established in two randomized, double-blind, active-controlled studies (PURPOSE 1 and PURPOSE 2). PURPOSE 1 was in 5,338 cisgender adolescent girls and young women between 16 and 25 years of age who had unknown HIV-1 status at screening and who were at risk of acquiring HIV-1 based on sexual activity with male partners. Participants were randomized to Yeztugo, Descovy, or Truvada. The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to Yeztugo compared with the rate of incident HIV-1 infections per 100 person-years in participants randomized to Truvada. Yeztugo demonstrated superiority with a 100% reduction in the risk of incident HIV-1 infection over Truvada. The incidence rate per 100 person-years was 0.00 with Yeztugo and 1.69 with Truvada (rate ratio 0.000, 95% CI: 0.000, 0.101; p < 0.0001). PURPOSE 2 was in 3,265 cisgender men, transgender women, transgender men, and gender nonbinary individuals 16 years of age and older who had unknown HIV-1 status at screening and who were at risk of acquiring HIV-1 based on sexual activity with male partners. Participants were randomized to Yeztugo or Truvada. The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to Yeztugo compared with the rate of incident HIV1 infections per 100 person-years in participants randomized to Truvada. Yeztugo demonstrated superiority with an 89% reduction in the risk of incident HIV-1 infection over Truvada. The incidence rate per 100 person-years was 0.1 with Yeztugo and 0.93 with Truvada (rate ratio 0.111, 95% CI: 0.024, 0.513; p = 0.00245). Yeztugo carries a boxed warning for risk of drug resistance with use of Yeztugo for HIV-1 PrEP in undiagnosed HIV-1 infection and is contraindicated in individuals with unknown or positive HIV-1 status.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Apretude (cabotegravir) is an HIV-1 integrase strand transfer inhibitor (INSTI) indicated in at-risk adults and adolescents weighing at least 35 kg for HIV-1 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, a two-drug co-packaged product of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI), and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI), is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 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.

Sunlenca, anHIV-1 capsid inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.

Yeztugo, an HIV-1 capsid inhibitor, is indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating Yeztugo.

References

1. Cabenuva [package insert]. Durham, NC: ViiV Healthcare. June 2025.
2. Swindells S, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression (ATLAS). n Engl J Med. 2020 March 382:1112-1123.
3. Orkin C, et al. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection (FLAIR). n Engl J Med. 2020 March 382:1124-1135.

4. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Updated May, 2025. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Accessed August 14, 2025.
5. Apretude [package insert]. Durham, NC: ViiV Healthcare. April 2025.
6. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. . https://stacks.cdc.gov/view/cdc/112360 Accessed August 14, 2025.
7. Landovitz R.J., et al. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women (HPTN 083). n Engl J Med. 2021 August 385:595-608.
8. Sunlenca [package insert]. Foster City, CA: Gilead Sciences, Inc. November 2024.
9. Yeztugo [Package Insert]. Foster City, CA: Gilead Sciences, Inc. June 2025.

Policy History/Revision Information

Date	Summary of Changes
11/01/2025	**Coverage Rationale** • Revised list of applicable long-acting injectable antiretroviral products; added Yeztugo (lenacapavir) • Added language to indicate: o This policy refers to Sunlenca injection and Yeztugo injection for administration by a healthcare professional; Sunlenca oral tablets and Yeztugo oral tablets are obtained under the pharmacy benefit o Yeztugo (lenacapavir) is proven to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents weighing at least 35kg o Yeztugo is medically necessary when the following additional criteria are met: ***Initial Therapy*** § Used for HIV-1 pre-exposure prophylaxis (PrEP) § Patient has a negative HIV-1 test § Provider confirms that the patient will be tested for HIV-1 infection with each subsequent injection § Dosing is in accordance with the U.S. FDA approved labeling § Initial authorization is for no more than 12 months ***Continuation of Therapy*** § Patient has previously received treatment with Yeztugo § Patient has a negative HIV-1 test § Provider confirms that the patient will be tested for HIV-1 infection with each subsequent injection § Dosing is in accordance with the U.S. FDA approved labeling § Authorization is for no more than 12 months o Yeztugo is unproven and not medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1) **Supporting Information** • Updated *Background*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version IEXD0103.15

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.