

lenacapavir (Yeztugo[®])

Policy # 00940

Original Effective Date: 09/01/2025

Current Effective Date: 09/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

Note: lenacapavir (Sunlenca[®]) is addressed separately in medical policy 00844.

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 lenacapavir (Yeztugo[®])[†] for pre-exposure prophylaxis (PrEP) of human immunodeficiency virus type 1 (HIV-1) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for lenacapavir (Yeztugo) will be considered when the following criteria are met:

- Patient is requesting Yeztugo for pre-exposure prophylaxis (PrEP) of HIV-1; AND
- Patient has a negative HIV-1 test prior to beginning therapy with Yeztugo; AND
- Patient weighs at least 35 kg; AND
- Patient is an adult or adolescent 16 years of age or older; AND
*(Note: Age greater than or equal to 16 is an additional Company requirement for coverage eligibility. Age 12 to 15 will be denied as not medically necessary** and age less than 12 will be denied as investigational.)*
- 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.)
- Patient is NOT using/planning to use lenacapavir (Yeztugo) in combination with other therapies approved for PrEP including, but not limited to, cabotegravir injection (Apretude), emtricitabine and tenofovir alafenamide (Descovy), or emtricitabine/tenofovir disoproxil fumarate (Truvada); AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- For Yeztugo 463.5 mg/1.5 mL (309 mg/mL) single-dose vial requests: requested dose is equal to 927 mg by subcutaneous injection every 6 months.

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of lenacapavir (Yeztugo) in patients aged 12 to less than 16 years of age to be **not medically necessary**.**

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 the use of lenacapavir (Yeztugo) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational**.*

Based on review of available data, the Company considers the use of lenacapavir (Yeztugo) in patients less than 12 years of age to be **investigational**.**

Based on review of available data, the Company considers the use of lenacapavir (Yeztugo) in combination with other therapies approved for PrEP to be **investigational**.**

Background/Overview

Yeztugo is an HIV-1 capsid inhibitor formulated as a long-acting injectable therapy for PrEP. It is available in 463.5 mg/1.5 mL (309 mg/mL) single-dose vials and 300 mg tablets. The recommended initiation dose is two subcutaneous (SC) injections (2 x 463.5 mg/mL) administered by a health care professional with two oral Yeztugo tablets (2 x 300 mg) on Day 1, followed by two oral Yeztugo tablets (2 x 300 mg) on Day 2; the continuation dose is two SC injections (2 x 463.5 mg/1.5 mL) once every 6 months. Anticipated missed injections can be covered with Yeztugo tablets (2 x 300 mg) once every 7 days for up to 6 months. Supplemental doses of Yeztugo are required if a strong or moderate inducer of cytochrome P450 3A is initiated. Yeztugo is contraindicated in individuals with unknown or positive HIV-1 status and carries a Boxed Warning regarding the risk of drug resistance in undiagnosed early HIV-1 infection. Lenacapavir is also available as Sunlenca^{®‡} (lenacapavir tablets and SC injection), which is indicated in combination with other antiretrovirals, for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant HIV-1.

Yeztugo is the fourth agent approved for HIV PrEP. It is the second long-acting injectable product, following Apretude, an integrase strand-transfer inhibitor (INSTI). Truvada^{®‡} and Descovy^{®‡}, both HIV-1 nucleoside reverse transcriptase inhibitors (NRTI), are oral formulations which are dosed once daily. All of the available PrEP agents are indicated to reduce the risk of sexually acquired HIV-1 infection in individuals ≥ 35 kg. Truvada, also available as generic emtricitabine/tenofovir disoproxil fumarate (FTC/TDF), is recommended for all populations at risk for HIV acquisition and for at-risk individuals who are pregnant or breastfeeding. Descovy is recommended for cisgender men and others whose exposures do not include receptive vaginal sex or injection drug use alone; it is recommended for the prevention of HIV-1 from vaginal exposures for those in whom FTC/TDF is contraindicated or undesirable. Apretude and Yeztugo are recommended for people likely to be

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exposed to HIV-1 sexually and for PrEP in pregnant persons according to the IAS-USA recommendations for the treatment and prevention of HIV in adults (2024). Data is insufficient to recommend Yeztugo during breastfeeding. At the time of Yeztugo discontinuation, alternative methods of HIV prevention are recommended beginning 6 months after the last injection if exposures are ongoing. Adherence to the prescribed treatment regimen is essential.

The US Preventative Services Task Force (USPTF) recommends PrEP using effective antiretroviral therapy in persons at increased risk of HIV-1 acquisition to decrease the risk of acquiring HIV-1. The USPTF recommends that PrEP be considered for the following persons: 1) Sexually active adults and adolescents ≥ 35 kg who have engaged in anal or vaginal sex in the past 6 months and have any of the following: 1) a sexual partner with HIV, a bacterial sexually transmitted infection in the past 6 months, or a history of inconsistent condom use with sex partner(s) whose HIV status is not known; or 2) persons who inject drugs and have a drug-injecting partner who has HIV or shares injection equipment. Effective formulations of PrEP are cited as FTC/TDF and Apretude in at-risk adults and adolescents ≥ 35 kg to reduce the risk of sexually acquired HIV-1 and Descovy in at-risk adults and adolescents ≥ 35 kg to reduce the risk of sexually acquired HIV-1, excluding individuals at risk from receptive vaginal sex. Yeztugo was not approved at the time recommendations were made. Despite no PrEP medications having approval for the indication of reducing the risk of acquiring HIV-1 via injection drug use, it is noted that such individuals are likely to benefit from PrEP with any FDA-approved PrEP medication. The Centers for Disease Control and Prevention (CDC) US Public Health Service Recommendations emphasize the importance of HIV-1 testing prior to prescribing PrEP and while taking PrEP. The CDC also recommends that all patients between the ages of 13 and 64 get tested for HIV at least once as part of routine health care. The CDC actively monitors HIV incidence and prevalence in adults and adolescents aged ≥ 13 years as part of the National HIV Surveillance System (NHSS). NHSS gathers this data to better understand the distribution of HIV among populations and communities and uses it to guide decisions about programs, policies, and resources.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Yeztugo was approved in June of 2025 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.

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 regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Yeztugo in reducing the risk of HIV-1 acquisition were evaluated in two randomized, double-blind, active-controlled, multinational trials (PURPOSE 1 and PURPOSE 2).

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PURPOSE 1

PURPOSE 1 enrolled cisgender adolescent girls and young women between 16 and 25 years of age in South Africa and Uganda 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 who tested negative for HIV-1 at screening and baseline were randomized to receive Yeztugo, once daily Descovy, or once daily Truvada in a 2:2:1 ratio. The median age of participants was 21 years (range, 16-26). 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. There were 55 incident HIV-1 infections observed in the trial; none in the Yeztugo group (0 per 100 person-years; 95% CI: 0.00, 0.19), 39 in the Descovy group (2.02 per 100 person-years; 95% CI: 1.44, 2.76), and 16 in the Truvada group (1.69 per 100 person-years; 95% CI: 0.96, 2.74). Yeztugo reduced the incidence of HIV-1 by 100% compared with the background HIV-1 incidence (incidence rate ratio 0.00; 95% CI: 0.00, 0.04; $P < 0.001$) and by 100% compared with FTC/TDF (incidence rate ratio 0.00; 95% CI: 0.00, 0.10; $P < 0.001$).

PURPOSE 2

PURPOSE 2 was in 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 who tested negative for HIV-1 at screening and baseline were randomized to receive Yeztugo or once daily Truvada in a 2:1 ratio. The median age of participants was 29 years (range, 17-74). 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. There were 11 incident HIV-1 infections during the trial; 2 in the Yeztugo group (0.10 per 100 person-years; 95% CI: 0.01, 0.37) and 9 in the Truvada group (0.93 per 100 person-years; 95% CI: 0.43, 1.77). The incidence of HIV-1 infection with Yeztugo was significantly lower than the background incidence rate (95% lower, incidence rate ratio 0.04; 95% CI: 0.01, 0.18; $P < 0.001$) and significantly lower than the incidence rate with Truvada (89% lower, incidence rate ratio 0.11; 95% CI: 0.02, 0.51; $P = 0.002$ for superiority).

References

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Policy History

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08/07/2025 Medical Policy Committee review

08/13/2025 Medical Policy Implementation Committee approval. New policy.

10/01/2025 Coding update.

08/12/2026 Pre Pharmacy & Therapeutics Committee review.

08/19/2026 Pharmacy & Therapeutics Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 08/2027

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT[®])[‡], copyright 2025 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 Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue 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 Louisiana Blue 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 Louisiana Blue Medical Policy 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.

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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 codes
HCPCS	J0738 Delete codes effective 09/01/2026: C9399, J0799
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.

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‡ 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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.