A NEW ERA IN PrEP

CLINICAL OVERVIEW

SAY YES TO 6 MONTHS OF HIV PROTECTION[1]

After initiation dosing.

Actor portrayals.

Now Approved

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

Go With Purpose

Indication

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

Important Safety Information

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF YEZTUGO IN UNDIAGNOSED HIV-1 INFECTION

- **Individuals must be tested for HIV-1 infection prior to initiating YEZTUGO, and with each subsequent injection of YEZTUGO, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of YEZTUGO by individuals with undiagnosed HIV-1 infection. Do not initiate YEZTUGO unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving YEZTUGO must transition to a complete HIV-1 treatment regimen.**

Please see additional Important Safety Information throughout and full Prescribing Information for **YEZTUGO**, including **BOXED WARNING**.

While great progress has been made, there were still over

new HIV diagnoses in the US in 2023.[2]

[a]CDC, 2023. Estimated HIV diagnoses in the US and 6 territories and free states for individuals aged ≥13 years.

More prevention strategies give you more ways to make a difference

High correlation proven between STI acquisition and HIV diagnosis[3-5]

~1 in 4 **individuals recently diagnosed with HIV had an STI within the 6 months prior to their diagnosis[4]**

(Truong HM, 2015; N=214. Study analyzed cases between 2005 and 2011 at publicly funded and community-based clinics in San Francisco)

STI history is one of the strongest indicators of potentially acquiring HIV[3-5]

Among MSM with a history of rectal gonorrhea or chlamydia,

1 in 7 **were diagnosed with HIV within a year[6]**

(Barbee LA, et al; 2017)

Make PrEP a part of every STI follow-up discussion and help protect people from HIV

PrEP medications do not reduce the risk of STIs other than HIV. PrEP medication should be considered part of a comprehensive STI prevention plan.[7]

MSM=men who have sex with men; PrEP=pre-exposure prophylaxis; STI=sexually transmitted infection.

YEZTUGO forms a drug depot beneath the skin, contributing to its longer action[1,8,9]

This is how the delivery system works:

1 Subcutaneous injection

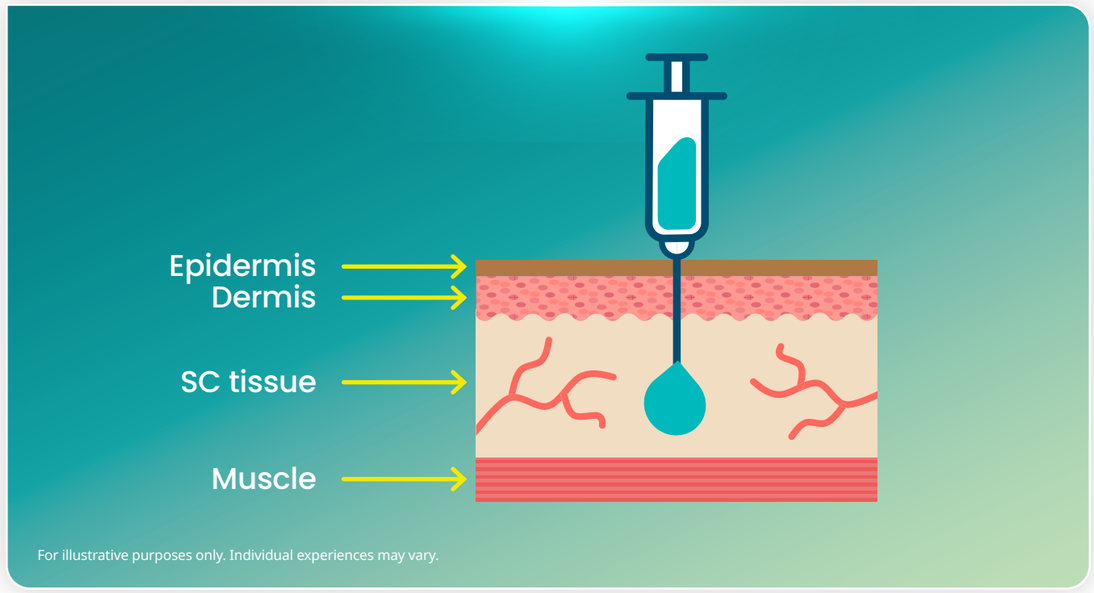
YEZTUGO is injected subcutaneously into an appropriate injection site.

2 Drug depot forms

After injection, YEZTUGO collects under the skin to form a drug depot.

3 Continuous release

The drug depot is how YEZTUGO can be slowly released over time.



SC=subcutaneous.

Important Safety Information (cont'd)

Contraindications

- YEZTUGO is contraindicated in individuals with unknown or positive HIV-1 status.

Warnings and precautions

- **Comprehensive risk management:**
  - Use YEZTUGO to reduce the risk of HIV-1 acquisition as part of a comprehensive prevention strategy including adherence to the administration schedule and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs).

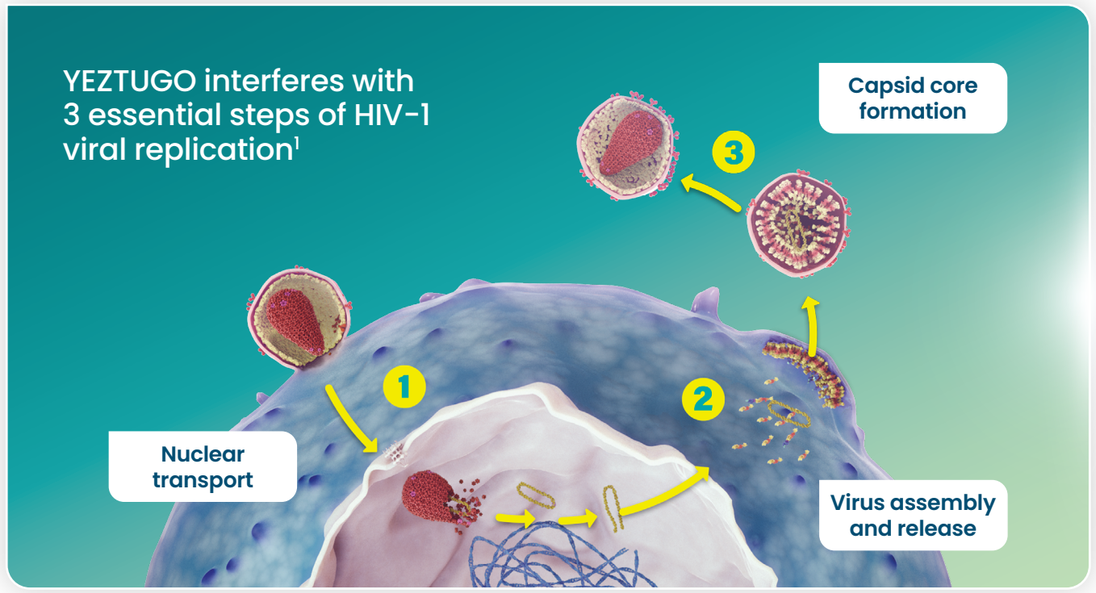
YEZTUGO is a first-in-class HIV-1 capsid inhibitor for PrEP[1,8,9]

YEZTUGO is the first-and-only HIV prevention option that targets the HIV-1 capsid at multiple stages of the virus life cycle[1,8,9]

Watch a video of YEZTUGO in action here.

How YEZTUGO works:

- The capsid core contains and protects viral RNA and enzymes for HIV replication[10]
- The HIV-1 viral life cycle is dependent on the function of the capsid at the following stages of HIV-1 replication: nuclear transport, virus assembly and release, and capsid core formation[1]
- YEZTUGO disrupts these stages in the HIV viral life cycle once HIV enters the body, resulting in an abnormal structure of the virus and, thus, inhibiting HIV-1 replication[1]



RNA=ribonucleic acid.

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Comprehensive risk management: (cont'd)**
  - HIV-1 acquisition risk includes behavioral, biological, or epidemiologic factors including, but not limited to, condomless sex, past or present STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high-prevalence area or network. Counsel individuals on the use of other prevention methods to help reduce their risk.

Please see additional Important Safety Information throughout and full Prescribing Information for YEZTUGO, including BOXED WARNING.

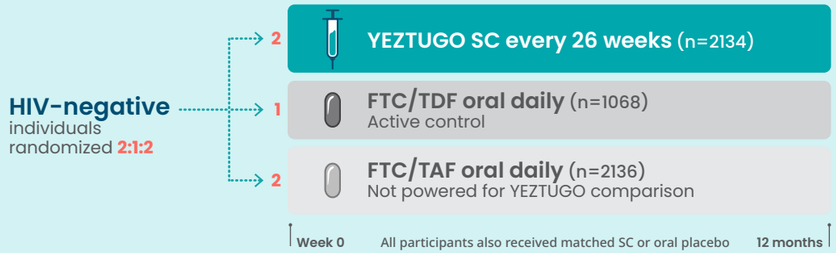
yeztugo® 463.5mg/1.5mL (lenacapavir) injection

The first phase 3 HIV prevention clinical trial to study pregnant and lactating women[1,8,11,a]

Key inclusion and eligibility criteria

- 16 to 25 years
- Cisgender adolescent girls and young women sexually active with male partners
- Individuals with likelihood of acquiring HIV,[b] and not on PrEP
- South Africa and Uganda

Study design



bHIV incidence was calculated for the screened population to avoid the need for a placebo group for ethical reasons

Primary analysis: Performed at a prespecified interim when 50% of participants completed 52 weeks, and the trial was stopped[c]

Efficacy endpoint: HIV incidence rate/100 PY

Primary efficacy analysis: HIV incidence rate with YEZTUGO vs bHIV

Secondary efficacy analysis: HIV incidence rate with YEZTUGO vs FTC/TDF

[a]The first phase 3 HIV prevention clinical trial to allow individuals to stay enrolled and continue on study drug if they became pregnant or started lactating.
[b]Eligible individuals had sexual encounters without recent HIV testing and had unknown HIV status.
[c]**The determination of efficacy was based on interim analyses when 50% of randomized participants completed 52 weeks of follow-up. Based on results, the study arms were unblinded, and this interim analysis became the primary analysis.**
bHIV=background HIV; FTC/TAF=emtricitabine/tenofovir alafenamide fumarate; FTC/TDF=emtricitabine/tenofovir disoproxil fumarate; PY=person-years.

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Comprehensive risk management: (cont'd)**
  - Use YEZTUGO only in individuals confirmed to be HIV-1 negative. Evaluate for current or recent signs or symptoms consistent with HIV-1 infection. Confirm HIV-1 negative status prior to initiating, prior to each subsequent injection, and as clinically appropriate.

Demographic and clinical characteristics of participants at baseline

Select characteristics	YEZTUGO N=2138	FTC/TDF N=1070
Age		
Median—yr (range)	21 (16–25)	21 (16–25)
16 or 17 yr—no. (%)	56 (2.6)	23 (2.1)
Black race—no. (%)[d]	2135 (99.9)	1068 (99.8)
Sexually transmitted infection—no. (%)		
Chlamydia trachomatis	520 (24.3)	263 (24.6)
Neisseria gonorrhoeae	197 (9.2)	90 (8.4)
Trichomonas vaginalis	154 (7.2)	82 (7.7)
Syphilis	57 (2.7)	29 (2.7)

[d]Race was reported by the participants. All non-Black participants were multiracial.
no.=number; yr=year.

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Potential risk of resistance:**
  - There is a potential risk of developing resistance to YEZTUGO if an individual acquires HIV-1 before or when receiving YEZTUGO, or following discontinuation. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection taking only YEZTUGO, because YEZTUGO alone is not a complete regimen for HIV-1 treatment.

Please see additional Important Safety Information throughout and full Prescribing Information for YEZTUGO, including BOXED WARNING.

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

The first phase 3 HIV prevention study to intentionally include gender-diverse individuals[1,9,12]

Key inclusion and eligibility criteria

Cisgender men, transgender women and men, nonbinary individuals, sexually active with male partners

16+ years

Individuals with likelihood of acquiring HIV,[a] and not on PrEP

Argentina, Brazil, Mexico, Peru, South Africa, Thailand, USA

Study design

bHIV incidence was calculated for the screened population to avoid the need for a placebo group for ethical reasons

Primary analysis: Performed at a prespecified interim when 50% of participants completed 52 weeks, and the trial was stopped[b]

Efficacy endpoint: HIV incidence rate/100 PY

Primary efficacy analysis: HIV incidence rate with YEZTUGO vs bHIV

Secondary efficacy analysis: HIV incidence rate with YEZTUGO vs FTC/TDF

[a]Eligible individuals had condomless sex, no recent HIV testing, and had unknown HIV status.
[b]**The determination of efficacy was based on interim analyses when 50% of randomized participants completed 52 weeks of follow-up. Based on results, the study arms were unblinded, and this interim analysis became the primary analysis.**

Demographic and clinical characteristics of participants at baseline

Select characteristics	YEZTUGO N=2183	FTC/TDF N=1088
Age		
Median—yr (range)	28 (17–74)	29 (17–73)
16 to ≤25 yr—no. (%)	752 (34.4)	344 (31.6)
Country—no. (%)		
Argentina	161 (7.4)	64 (5.9)
Brazil	769 (35.2)	396 (36.4)
Mexico	8 (0.4)	4 (0.4)
Peru	309 (14.2)	138 (12.7)
South Africa	246 (11.3)	112 (10.3)
Thailand	250 (11.5)	139 (12.8)
United States	440 (20.2)	235 (21.6)

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Potential risk of resistance: (cont'd)**
  - To minimize this risk, it is essential to test before each injection and additionally as clinically appropriate. Individuals confirmed to have HIV-1 must immediately begin a complete HIV-1 treatment regimen.
  - Alternative forms of PrEP should be considered after discontinuation of YEZTUGO for those who are at continuing risk of HIV-1 acquisition and should be initiated within 28 weeks of the last YEZTUGO injection.

Please see additional Important Safety Information throughout and full Prescribing Information for **YEZTUGO, including BOXED WARNING.**

yeztugo® 463.5mg/1.5mL (lenacapavir) injection

The first phase 3 HIV prevention study to intentionally include gender-diverse individuals[1,9,12]

Demographic and clinical characteristics of participants at baseline (cont'd)

Select characteristics	YEZTUGO N=2183	FTC/TDF N=1088
Race or ethnic group—no./total no. (%)[a]		
Asian	269/2175 (12.4)	144/1086 (13.3)
Black	811/2175 (37.3)	420/1086 (38.7)
Indigenous or Indigenous ancestry	341/2175 (15.7)	156/1086 (14.4)
White	722/2175 (33.2)	344/1086 (31.7)
Other and other multiracial	32/2175 (1.5)	22/1086 (2.0)
Hispanic or Latine	1378/2182 (63.2)	675/1088 (62.0)
Gender identity—no. (%)		
Cisgender man	1697 (77.7)	846 (77.8)
Transgender woman	315 (14.4)	161 (14.8)
Transgender man	29 (1.3)	14 (1.3)
Gender nonbinary[b]	136 (6.2)	63 (5.8)
Other[c]	6 (0.3)	4 (0.4)

[a]Race and ethnic group were reported by the participants. The "Black" category included all of the participants who identified as being Black or as being of Black ancestry and included the terms "Black," "Black/White," "Black/Pardo" (Brazilian term for a specific racial category), "Black/Brown" (Brazil), "Black/Colored" (South African term for a specific racial category), "Black/American Indian or Alaska Native," "Black/Asian," and "Black/Native Hawaiian or Pacific Islander." The "Indigenous or Indigenous ancestry" category included the terms "American Indian or Alaska Native," "Native Hawaiian or Pacific Islander," "Asian/Native Hawaiian or Pacific Islander," "White/Native Hawaiian or Pacific Islander," and "White/American Indian or Alaskan Native." The "other and other multiracial" category included the terms "Asian/White," "Colored" (South Africa), "Pardo" (Brazil), "White/Brown" (Brazil), "multiracial any other," and "not multiracial other."
[b]Among the participants who identified as gender nonbinary, 122 (89.7%) in the YEZTUGO group and 53 (84.1%) in the FTC/TDF group were assigned male at birth.
[c]The "other" category included participants who identified as "Travesti" (3 participants in the YEZTUGO group and 3 in the FTC/TDF group) or as an "other" gender (3 in the YEZTUGO group and 1 in the FTC/TDF group).

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Long-acting properties and potential associated risks:**
  - Residual concentrations of YEZTUGO may remain in systemic circulation for up to 12 months or longer after the last injection.

Demographic and clinical characteristics of participants at baseline (cont'd)

Select characteristics	YEZTUGO N=2183	FTC/TDF N=1088
No previous HIV testing—no. (%)	597 (27.3)	306 (28.1)
Median time since last HIV test—mo. (range)[d]	7.2 (2.6-149.4)	7.1 (1.2-274.2)
Any previous use of PrEP—no. (%)	515 (23.6)	249 (22.9)
Median time since last use of PrEP—mo. (range)[e]	13.0 (0.7-103.9)	10.8 (0.7-274.5)
Condomless receptive anal sex with ≥2 partners in previous 12 wks—no. (%)	2128 (97.5)	1049 (96.4)
Sexually transmitted infection—no. (%)[f]		
Chlamydia trachomatis	253 (11.6)	126 (11.6)
Neisseria gonorrhoeae	193 (8.8)	115 (10.6)
Syphilis	84 (3.8)	43 (4.0)
Use of gender-affirming hormone therapy—no. (%)[g]	253 (11.6)	131 (12.0)

[d]Data are included for 1585 participants in the YEZTUGO group and 782 in the FTC/TDF group.
[e]Included are participants who were not taking PrEP at baseline (449 in the YEZTUGO group and 215 in the FTC/TDF group).
[f]*Chlamydia trachomatis* and *Neisseria gonorrhoeae* diagnoses were based on testing of pharyngeal, rectal, and urethral (urine) samples, performed by central and local laboratories. Blood testing for syphilis was performed locally with the use of local testing protocols.
[g]Use of gender-affirming hormone therapy included concomitant use with the trial regimen during the randomized, blinded phase.
wk=week.

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Long-acting properties and potential associated risks: (cont'd)**
  - Select individuals who agree to the required injection dosing schedule because nonadherence or missed doses could lead to HIV-1 acquisition and development of resistance.

Please see additional Important Safety Information throughout and full Prescribing Information for YEZTUGO, including BOXED WARNING.

yeztugo® 463.5mg/1.5mL (lenacapavir) injection

EFFICACY

YEZTUGO showed superior efficacy compared to FTC/TDF[1,8,9]

PURPOSE 1

At the time of primary analysis[a]

100%

of participants **remained HIV negative** while on YEZTUGO compared to **98.5%** on FTC/TDF

YEZTUGO (N=2134)	FTC/TDF (N=1068)
0 HIV acquisitions	**16 HIV acquisitions**

PURPOSE 1 included cisgender adolescent girls and young women.[8]

Efficacy endpoint: HIV incidence rate/100 PY

- **Primary efficacy analysis:** HIV incidence rate with YEZTUGO (0/100 PY) was significantly lower than bHIV (2.41/100 PY), IRR (95% CI): 0.000 (0.000, 0.042), p<0.0001[1,8]
- **Secondary efficacy analysis:** HIV incidence rate with YEZTUGO (0/100 PY) was significantly lower than FTC/TDF (1.69/100 PY), IRR (95% CI): 0.000 (0.000, 0.101), p<0.0001[1,8]

[a]**The determination of efficacy was based on interim analyses when 50% of randomized participants completed 52 weeks of follow-up. Based on results, the study arms were unblinded, and this interim analysis became the primary analysis.**
CI=confidence interval; IRR=incidence rate ratio.

PURPOSE 2

At the time of primary analysis[b]

99.9%

of participants **remained HIV negative** while on YEZTUGO compared to **99.2%** on FTC/TDF

YEZTUGO (N=2179)	FTC/TDF (N=1086)
2 HIV acquisitions	**9 HIV acquisitions**

PURPOSE 2 included cisgender men, transgender men and women, and nonbinary persons.[9]

Efficacy endpoint: HIV incidence rate/100 PY

- **Primary efficacy analysis:** HIV incidence rate with YEZTUGO (0.1/100 PY) was significantly lower than bHIV (2.37/100 PY), IRR (95% CI): 0.043 (0.010, 0.182), p<0.0001[1,9]
- **Secondary efficacy analysis:** HIV incidence rate with YEZTUGO (0.1/100 PY) was significantly lower than FTC/TDF (0.93/100 PY), IRR (95% CI): 0.111 (0.024, 0.513), p=0.00245[1,9]

[b]**The determination of efficacy was based on interim analyses when 50% of randomized participants completed 52 weeks of follow-up. Based on results, the study arms were unblinded, and this interim analysis became the primary analysis.**

Important Safety Information (cont'd)

Warnings and precautions (cont'd)

- **Serious injection site reactions:** Improper administration (intradermal injection) has been associated with serious injection site reactions, including necrosis and ulcer. Only administer YEZTUGO subcutaneously.

Important Safety Information (cont'd)

Adverse reactions

- **Most common adverse reactions (≥5%)** in YEZTUGO clinical trials were injection site reactions, headache, and nausea.

Please see additional Important Safety Information throughout and full Prescribing Information for **YEZTUGO, including BOXED WARNING.**

yeztugo® 463.5mg/1.5mL (lenacapavir) injection

Safety evaluated in 2 large clinical studies[1]

Adverse reactions (all grades) reported in ≥2%[a] of participants receiving YEZTUGO in PURPOSE 1 or PURPOSE 2

Adverse reaction	PURPOSE 1		PURPOSE 2	
	YEZTUGO N=2140	FTC/TDF[b] N=1070	YEZTUGO N=2183	FTC/TDF[b] N=1088
Injection site reactions	69%	34%	83%	69%
Headache	7%	8%	2%	2%
Nausea	5%	11%	2%	4%
Dizziness	4%	6%	<1%	1%
Vomiting	4%	7%	<1%	1%
Diarrhea	4%	4%	2%	2%

Low discontinuations due to AEs (all cause) with YEZTUGO[c]

PURPOSE 1	PURPOSE 2
<1%	1%

[a]Frequencies of ARs are based on all AEs attributed to study drug (or to the procedure for injection site reactions) by the investigator.
[b]Participants received placebo subcutaneous injections (polyethylene glycol 400).
[c]Percentage of participants in PURPOSE 1 who discontinued due to AEs (all cause): FTC/TDF <1%. Percentage of participants in PURPOSE 2 who discontinued due to AEs (all cause): FTC/TDF <1%.
AE=adverse event; AR=adverse reaction.

Important Safety Information (cont'd)

Drug interactions

- Strong or moderate CYP3A inducers may significantly decrease YEZTUGO concentrations. Dosage modifications are recommended when initiating these inducers.

Majority of ISRs were mild or moderate[1]

No serious ISRs occurred in either PURPOSE 1 or PURPOSE 2

Injection site reactions All grades reported in ≥2%[d,e]	PURPOSE 1		PURPOSE 2	
	YEZTUGO N=2140	FTC/TDF[f] or FTC/TAF[f] N=3205	YEZTUGO N=2183	FTC/TDF[f] N=1088
Nodule	64%	17%	63%	39%
Pain	31%	24%	56%	53%
Induration	4%	<1%	16%	10%
Swelling	4%	5%	7%	10%
Pruritus	2%	1%	3%	3%
Erythema	1%	1%	17%	19%
Bruising	<1%	<1%	3%	4%
Warmth	<1%	<1%	2%	2%

YEZTUGO overall ISRs by grade, n (%)	PURPOSE 1	PURPOSE 2
Grade 1 (mild)	1060 (50)	1441 (66)
Grade 2 (moderate)	406 (19)	361 (17)
Grade 3 (severe)	4 (0.2) *(included ulcer and nodule)*	14 (0.6) *(included ulcer, pain, erythema, edema, and dermatitis)*

[d]Participants receiving YEZTUGO in either PURPOSE 1 or PURPOSE 2.
[e]Frequencies are based on all injection site reactions attributed to study drug (or to the procedure) by the investigator.
[f]Participants received placebo subcutaneous injections (polyethylene glycol 400).
ISR=injection site reaction.

Important Safety Information (cont'd)

Drug interactions (cont'd)

- It is not recommended to use YEZTUGO with combined P-gp, UGT1A1, and strong CYP3A inhibitors.

Please see additional Important Safety Information throughout and full Prescribing Information for YEZTUGO, including BOXED WARNING.

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

DOSING

Straightforward dosing with twice-yearly YEZTUGO[1]

YEZTUGO is the first-and-only PrEP option that offers twice-yearly, in-office subcutaneous injections

Confirm HIV-1 negative status prior to injecting YEZTUGO and additionally as clinically appropriate.
In addition, counsel individuals about the importance of adherence to scheduled YEZTUGO dosing visits.

Initiating YEZTUGO

On Day 1 of initiation, you'll have the individuals take 2 tablets by mouth in addition to 2 subcutaneous injections in your office, then send them home with 2 tablets to be taken the next day.[a]

After that, it's just 2 injections 2 times a year.[b]

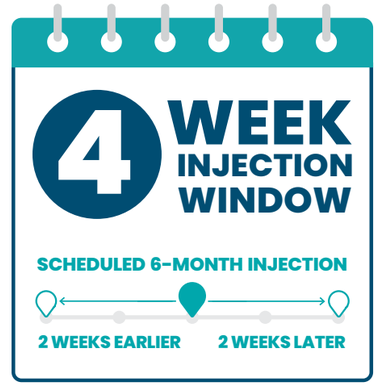
No oral dose after initial 2-day dosing

= 600 mg orally (2 x 300-mg tablets) = 927-mg subcutaneous injection (2 x 1.5-mL injections)

[a]Tablets may be taken with or without food.
[b]Unless the injection schedule is interrupted.

Flexible continuation dosing

YEZTUGO offers a ±2-week range on either side of the individual's target continuation dose, which is 26 weeks after the last injection, allowing for flexibility in scheduling for both your practice and the individuals you see.



Click here to watch a series of videos on dosing and administration.

Interested in a daily oral option? Click here to learn more.

Managing delayed and/or missed doses

If an individual is not able to stay on schedule—whether due to an anticipated delay or a missed injection or oral dose—there are options that may help them avoid interrupting YEZTUGO. See full Prescribing Information for complete details about each option.

Important Safety Information (cont'd)

Drug interactions (cont'd)

- Coadministration of YEZTUGO with sensitive substrates of CYP3A or P-gp may increase their concentrations and result in the increased risk of their adverse events. YEZTUGO may increase the exposure of drugs primarily metabolized by CYP3A initiated within 9 months after the last injection of YEZTUGO.

Important Safety Information (cont'd)

Dosage and administration

- **HIV screening:** Test for HIV-1 infection prior to initiating, prior to each subsequent injection, and as clinically appropriate using an approved or cleared test for the diagnosis of acute or primary HIV-1 infection.

Please see additional Important Safety Information throughout and full Prescribing Information for YEZTUGO, including BOXED WARNING.

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

DOSING

YEZTUGO dosing recommendations when initiating strong or moderate CYP3A inducers[1]

Maintain scheduled continuation injection dosing

Continue to administer once-every-6-months scheduled continuation dosing of YEZTUGO 927 mg subcutaneously (2 x 1.5-mL injections), plus administer supplemental doses of YEZTUGO as shown in the following tables.

Strong CYP3A Inducers: Schedule for Supplemental Doses of YEZTUGO[a]

Time	Dosage
On the day a strong CYP3A inducer is initiated (which should be at least 2 days after YEZTUGO is first initiated)	Supplemental dosage: Step 1 **927 mg subcutaneously** (2 x 1.5-mL injections) AND **600 mg orally** (2 x 300-mg tablets)
On the day after a strong CYP3A inducer is initiated	Supplemental dosage: Step 2 **600 mg orally** (2 x 300-mg tablets)
If a strong CYP3A inducer is coadministered for longer than 6 months	Subsequent supplemental dosage Every 6 months[b] from initiation of a strong CYP3A inducer, continue to administer supplemental doses of YEZTUGO as described above in Steps 1 and 2

After stopping the strong CYP3A inducer, continue the once-every-6-months scheduled continuation injection dosing of YEZTUGO.

[a]Dosing recommendations are not available for the initiation of YEZTUGO in individuals already receiving strong CYP3A inducers, nor in individuals receiving the weekly oral dosage of YEZTUGO (see: Managing delayed and/or missed doses).
[b]26 weeks ±2 weeks.

Moderate CYP3A Inducers: Schedule for Supplemental Doses of YEZTUGO[c]

Time	Dosage
On the day a moderate CYP3A inducer is initiated	Supplemental dosage **463.5 mg subcutaneously** (1 x 1.5-mL injection)
If a moderate CYP3A inducer is coadministered for longer than 6 months	Subsequent supplemental dosage Every 6 months[d] from initiation of a moderate CYP3A inducer, continue to administer supplemental dose of YEZTUGO as described above

After stopping the moderate CYP3A inducer, continue the once-every-6-months scheduled continuation injection dosing of YEZTUGO.

[c]Dosing recommendations are not available for the initiation of YEZTUGO in individuals already receiving moderate CYP3A inducers, nor in individuals receiving the weekly oral dosage of YEZTUGO (see: Managing delayed and/or missed doses).
[d]26 weeks ±2 weeks.
CYP3A=cytochrome P450 3A.

Drug interactions

Please see the full Prescribing Information for more details on drug interactions with YEZTUGO.

- **Strong or moderate inducers of CYP3A** may significantly decrease plasma concentrations of lenacapavir, which may reduce the effectiveness of YEZTUGO. Dosage modifications are recommended when initiating these inducers
- **Combined P-gp, UGT1A1, and strong CYP3A inhibitors** may significantly increase plasma concentrations of YEZTUGO. Concomitant administration with YEZTUGO is not recommended
- **YEZTUGO is a moderate inhibitor of CYP3A and a P-gp inhibitor** that may increase the concentrations of coadministered sensitive substrates of CYP3A and P-gp, and increase risk of their adverse events. See the prescribing information of these sensitive substrates for dosing recommendations or appropriate monitoring of safety. YEZTUGO may increase the exposure of drugs primarily metabolized by CYP3A initiated within 9 months after the last subcutaneous dose of YEZTUGO

Important Safety Information (cont'd)

Dosage and administration (cont'd)

- **Dosage:** Initiation dosing (injections and tablets) followed by once-every-6-months continuation injection dosing. Tablets may be taken with or without food.
  - **Initiation:** Day 1: 927 mg by subcutaneous injection (2 x 1.5-mL injections) and 600 mg orally (2 x 300-mg tablets). Day 2: 600 mg orally.
  - **Continuation:** 927 mg by subcutaneous injection every 6 months (26 weeks) from date of last injection ±2 weeks.

Please see additional Important Safety Information throughout and full Prescribing Information for YEZTUGO, including BOXED WARNING.

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

Overview of administering YEZTUGO[1]

6 key steps for every 6-month injection

Please see full Prescribing Information and Instructions for Use for more details on how to administer YEZTUGO.

Consider applying an ice pack prior to injections.[a]

YEZTUGO is administered in office via 2 x 1.5-mL subcutaneous injections in the appropriate injection sites.

Improper administration (intradermal injection) of lenacapavir has been associated with serious injection site reactions. Ensure YEZTUGO is only administered subcutaneously.

[a]This consideration for injections is not specific to YEZTUGO. Follow the protocols for your institution.

Setting expectations with individuals in your care when prescribing YEZTUGO

Talk with individuals about their injection schedule

- YEZTUGO is given every 6 months (26 weeks). Each dose is 2 injections
- On their first day with YEZTUGO, their starter doses will include 2 pills taken by mouth (with or without food), along with 2 injections given at their healthcare provider's office
- This is followed by 2 more pills taken at home the next day (with or without food)
- After that, they will get their injections every 6 months
- Remind them that they will need to have a negative HIV-1 test prior to starting YEZTUGO, before each injection, and when their healthcare provider tells them

Educate individuals about possible side effects

- The most common side effects are injection site reactions, headache, and nausea. Additional side effects listed on page 8
- Some people may notice or feel a bump (lump) at the injection site, while others may not
- Potential injection site reactions may include a bump, pain, skin hardening, swelling, itching, redness, bruising, or warmth
- Remind them to contact you if they experience any side effects

Remind individuals that staying on schedule is key to HIV prevention

- Each follow-up dose can be scheduled up to 2 weeks before or 2 weeks after their 6-month mark, which means 6 months (or 26 weeks) after the date of their last injection
- If they are not able to stay on schedule, let them know there are options that may help them avoid interrupting YEZTUGO. As a provider, you can learn more about these options in the full Prescribing Information

What to recommend to individuals

- Suggest setting more than 1 reminder for injection visits
- Plan ahead: Verify that the 6-month visit fits their schedule
- Consider reaching out to them before the 6-month follow-up injection date, and remind them to contact you immediately for any missed injections

See Patient Counseling Information in the full Prescribing Information for further details.

Important Safety Information (cont'd)

Dosage and administration (cont'd)

- **Anticipated delayed injections:** If scheduled 6-month injection is anticipated to be delayed by more than 2 weeks, YEZTUGO tablets may be taken on an interim basis (for up to 6 months) until injections resume. Dosage is 300 mg orally (1 x 300-mg tablet) once every 7 days. Resume continuation injections within 7 days of the last oral dose.

Please see additional Important Safety Information throughout and full Prescribing Information for **YEZTUGO**, including **BOXED WARNING**.

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

Multiple ways to acquire YEZTUGO

YEZTUGO offers flexibility in acquisition options for your practice

Specialty pharmacy

If your patient's insurance permits YEZTUGO to be dispensed via specialty pharmacy (SP), a specialty pharmacy can help with the steps to get your patient's prescribed medication shipped to you. Regardless of how the YEZTUGO components (oral tablets and injections) are covered, whether under pharmacy or medical benefit, the designated SP can support coordination and shipment.

In-house specialty pharmacy

If your practice has an in-house specialty pharmacy that is able to dispense the patient's medication, they may be able to acquire YEZTUGO from any of the in-network specialty distributors.

Buy and bill

If you choose to, and your patient's insurance covers YEZTUGO under medical benefit, you may be able to acquire YEZTUGO for in-office administration through the buy-and-bill process via any of the in-network specialty distributors.

If you are not able to administer YEZTUGO in your office, you can also refer your patients to alternative sites of care (ASOC).

Click here to see more information about acquiring YEZTUGO.

Gilead Advancing Access® is here to help

Dedicated program specialists are available to offer support

Advancing Access program offerings include:

Benefits investigation

Program may help research and verify the individual's insurance coverage for their prescribed Gilead medication and receive information on in-network pharmacy restrictions.

Prior authorization information

Program provides information if individual's insurance company requires the completion of a prior authorization for Gilead medication.

Medication Assistance Program

Eligible uninsured individuals may receive their Gilead medication for free through the Medication Assistance Program (MAP).

Co-pay support

The Gilead Co-pay Savings Program may help eligible, commercially insured individuals lower their out-of-pocket costs.[a] People enrolled in government prescription drug programs, such as Medicare Part D and Medicaid, are not eligible for the co-pay coupon. Restrictions may apply. Subject to change.

Advancing Access specialists can help provide insurance information support, including determining prior authorization and appeals process requirements, and connect people to available resources to help them navigate coverage.

They can also help individuals prescribed YEZTUGO to understand and navigate health insurance and Gilead medication costs. For more information, you can direct individuals to visit **PrEP.AdvancingAccess.com/hcp**, or call 1-800-226-2056.

Eligible individuals could pay as little as **$0** for YEZTUGO.[a]

[a]Co-pay coupon support is available for commercially insured eligible patients only. Additional restrictions may apply. Subject to change; for full terms and conditions, visit **GileadAdvancingAccess.com/copay-coupon-card**. This is not health insurance.

Click here to learn more about Advancing Access.

Important Safety Information (cont'd)

Dosage and administration (cont'd)

- **Missed injections:** If more than 28 weeks have elapsed since the last injection and YEZTUGO tablets have not been taken, restart with initiation dosing if clinically appropriate.
- Dosage modifications of YEZTUGO are recommended when initiating with strong or moderate CYP3A inducers. Consult the full Prescribing Information for recommendations.

Please see additional Important Safety Information throughout and full Prescribing Information for **YEZTUGO, including BOXED WARNING.**

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

yeztugo® (lenacapavir) injection 463.5mg/1.5mL

Deliver 6 months of HIV prevention with the only twice-yearly PrEP option[1]

Initiation injections + **Initiation tablets**

Rx YEZTUGO 463.5 mg/ 1.5-mL injection

Inject 3 mL (two 1.5-mL injections) subcutaneously on Day 1 (Day Supply: 180)

Quantity: *3 mL (1.5 mL x 2)*

Rx YEZTUGO 300-mg tablets

Take 2 tablets by mouth once on Day 1, and 2 tablets once on Day 2.

Quantity: *4 tablets*

Continuation injections only

Rx YEZTUGO 463.5 mg/ 1.5-mL injection

Inject 3 mL (two 1.5-mL injections) subcutaneously every 6 months from the date of last injection.

Quantity: *3 mL (1.5 mL x 2)*

For illustrative purposes only.

Indication

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

Learn more at YEZTUGOhcp.com.

Important Safety Information

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF YEZTUGO IN UNDIAGNOSED HIV-1 INFECTION

- **Individuals must be tested for HIV-1 infection prior to initiating YEZTUGO, and with each subsequent injection of YEZTUGO, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of YEZTUGO by individuals with undiagnosed HIV-1 infection. Do not initiate YEZTUGO unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving YEZTUGO must transition to a complete HIV-1 treatment regimen.**

Please see additional Important Safety Information throughout and full Prescribing Information for **YEZTUGO, including BOXED WARNING.**

References

1. YEZTUGO. Prescribing information. Gilead Sciences, Inc.; 2025. **2.** Centers for Disease Control and Prevention. Diagnoses, deaths, and prevalence of HIV in the United States and 6 territories and freely associated states, 2023. April 29, 2025. Accessed May 12, 2025. https://www.cdc.gov/hiv-data/media/files/2025/04/hiv_surv_rep_figures_2023.pptx **3.** Pathela P, Braunstein SL, Blank S, Schillinger JA. HIV incidence among men with and those without sexually transmitted rectal infections: estimates from matching against an HIV case registry. *Clin Infect Dis.* 2013;57(8):1203-1209. doi:10.1093/cid/cit437 **4.** Truong HM, Pipkin S, O'Keefe KJ, et al. Brief report: recent infection, sexually transmitted infections, and transmission clusters frequently observed among persons newly diagnosed with HIV in San Francisco. *J Acquir Immune Defic Syndr.* 2015;69(5):606-609. doi:10.1097/QAI.0000000000000681 **5.** Pathela P, Braunstein SL, Blank S, Shepard C, Schillinger JA. The high risk of an HIV diagnosis following a diagnosis of syphilis: a population-level analysis of New York City men. *Clin Infect Dis.* 2015;61(2):281-287. doi:10.1093/cid/civ289 **6.** Barbee LA, Khosropour CM, Dombrowksi JC, Golden MR. New human immunodeficiency virus diagnosis independently associated with rectal gonorrhea and chlamydia in men who have sex with men. *Sex Transm Dis.* 2017;44(7):385-389. doi:10.1097/OLQ.0000000000000614 **7.** Centers for Disease Control and Prevention. Clinical guidance for PrEP. February 10, 2025. Accessed May 12, 2025. https://www.cdc.gov/hivnexus/hcp/prep/index.html **8.** Bekker LG, Das M, Abdool Karim Q, et al; PURPOSE 1 study team. Twice-yearly lenacapavir or daily F/TAF for HIV prevention in cisgender women. *N Engl J Med.* 2024;391(13):1179-1192. doi:10.1056/NEJMoa2407001 **9.** Kelley CF, Acevedo-Quiñones M, Agwu AL, et al; PURPOSE 2 study team. Twice-yearly lenacapavir for HIV prevention in men and gender-diverse persons. *N Engl J Med.* 2025;392(13):1261-1276. doi:10.1056/NEJMoa2411858 **10.** Engelman A, Cherepanov P. The structural biology of HIV-1: mechanistic and therapeutic insights. *Nat Rev Microbiol.* 2012;10(4):279-290. doi:10.1038/nrmicro2747 **11.** Full efficacy and safety results for Gilead investigational twice-yearly lenacapavir for HIV prevention presented at AIDS 2024. News release. Gilead Sciences, Inc.; July 24, 2024. Accessed March 27, 2025. https://www.gilead.com/news/news-details/2024/full-efficacy-and-safety-results-for-gilead-investigational-twice-yearly-lenacapavir-for-hiv-prevention-presented-at-aids-2024 **12.** Gallardo-Cartagena J, Phanuphak N, Ndlovu N, et al. Global racial, ethnic, and gender diversity among participants enrolled in the PURPOSE 2 trial of lenacapavir for pre-exposure prophylaxis. Presented at: 5th HIV Research for Prevention Conference (HIVR4P 2024); October 6-10, 2024; Lima, Peru.

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