# YEZTUGO® (lenacapavir) for HIV-1 PrEP

**Navigating the US Prescribing Information** 

### **Disclaimers**

This non-promotional, proactive deck is intended to be used by Gilead Medical Affairs as educational material only.

This deck should only be presented by a Gilead employee, not a third-party speaker.

These slides provide only a summary and select sections of the FDA-approved YEZTUGO® US Prescribing Information.

Please see full Prescribing Information for YEZTUGO, including Boxed Warning, available at Gilead.com.



### **Boxed Warning**

# WARNING: RISK OF DRUG RESISTANCE WITH USE OF YEZTUGO FOR HIV-1 PrEP 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.

[see Dosage and Administration (2.1), Contraindications (4) and Warnings and Precautions (5.1, 5.2)]



# 1. Indications and Usage

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#### FULL PRESCRIBING INFORMATION

WARNING: RISK OF DRUG RESISTANCE WITH USE OF YEZTUGO FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (P/EP) IN UNDIAGNOSED HIV-1 INFECTION

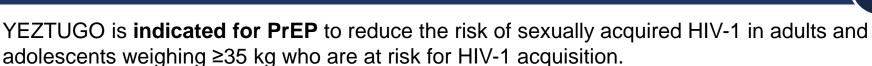
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status is confirmed. Individuals who acquire HIV-I while receiving YEZTUGO must transition to a complete HIV-1 treatment regimen [see Dosage and Administration (2.1), Contraindications (4), Warnings and Precautions (5.1, 5.2).

YEZTUGO is indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of Sexually acquired HIV. In adults and adolescents weighing at least 35 kg who are at sexually acquired HIV-1 in adults and adolescents weighing at least so by who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to inflating TISK TOT HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to maining YEZTUGO [see Dosage and Administration (2.1) and Warnings and Precautoris (3.1)]

### DOSAGE AND ADMINISTRATION

HIV-1 Screening for Individuals Receiving YEZTUGO for HIV-1

#### 1 Indications and Usage



Individuals must have a **negative HIV-1 test result** prior to initiating YEZTUGO.

[see Dosage and Administration (2.1) and Warnings and Precautions (5.1)]



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#### FULL PRESCRIBING INFORMATION

WARNING: RISK OF DRUG RESISTANCE WITH USE OF YEZTUGO FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (P/EP) 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 (see Dosage and Administration (2.1), Contraindications (4), Warnings and Precautions (5.1, 5.2).

- YEZTUGO is indicated for pre-exposure prophylaxis (PyEP) to reduce the risk of Sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at Sexually acquired THV-1 in adults and adolescents weighing a least 50 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 est prior to inland, TISK TOT HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to infamily YEZTUGO [see Dosage and Administration (2.1) and Warnings and Precautoris (3.1).
- DOSAGE AND ADMINISTRATION

### 2.1 HIV-1 Screening for Individuals Receiving YEZTUGO



Screen all individuals for HIV-1 prior to initiating YEZTUGO, prior to each subsequent injection of YEZTUGO, and additionally as clinically appropriate, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. [see Indications and Usage (1), Contraindications (4) and Warnings and Precautions (5.1, 5.2) and Clinical Studies (14)]



Prior to initiating YEZTUGO: Negative result from an Ag/Ab-specific test should be confirmed using an RNA-specific assay.<sup>a</sup>

Prior to continuing YEZTUGO: Negative result from a rapid, point-of-care Ag/Ab test should be confirmed using a more sensitive assay.

#### 2.2 Adherence to YEZTUGO



Prior to starting YEZTUGO, healthcare providers should select individuals who agree to the required testing and Q6M injection dosing schedule, and counsel individuals about the importance of adherence to scheduled YEZTUGO dosing visits.

[see Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2) and Microbiology (12.4)]

<sup>a</sup>Even if the results of the RNA-assay are available after YEZTUGO initiation Ag/Ab, antigen/antibody; Q6M, every 6 months



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Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2), and

The YEZTUGO dosing schedule in adults and adolescents weighing at least 35 ig consists of a required initiation dosing (subcutaneous njections and oral tables) followed by once every 6-months continuation dosing (subcutaneous injections)

Dosing Schedule for YEZTUGO Initiation and Continuation in Adults

(Table 1). YEZTUGO oral tablets may be taken with or without food

and Adolescents Weighing at Least 35 kg

Microbiology (12.4)].

2.3 Recommended Dosage

[see Clinical Pharmacology (12.3)].

From the date of the last injection.

Dosing Schedule for Missed Dose

If the Day 2 oral initiation dose (600 mg, see Table 1) is missed, take it as soon as need to be careed the control of the careed the sound of the sound of

During continuation dosing, if the scheduled 6-month injection is anticrated to be (a) the scheduled 6-month injection is an interm basis (b) the scheduled 6-month injection in a beta when the discrete delayed by more than 2 weeks, YEZTUGO tablets may be taken on an interm basis (b) the schedule of th

If the Uay 2 oral inhabition dose (600 mg, see Table 1) is missed, take it as so, possible. Do not take Day 1 and Day 2 oral initiation doses on the same day.

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#### 2.3 Recommended Dosage



The YEZTUGO dosing schedule in adults and adolescents weighing ≥35 kg consists of a required initiation dosing (SC injections and oral tablets) followed by Q6M continuation dosing (SC injections) (Table 1).

YEZTUGO oral tablets may be taken with or without food.

[see Clinical Pharmacology (12.3)]

Table 1. Dosing Schedule for YEZTUGO Initiation and Continuation<sup>a</sup>

Time	
	Dosage of YEZTUGO: Initiation <sup>b</sup>
Day 1	927 mg by SC injection (2 × 1.5 mL injections)
	600 mg orally (2 × 300 mg tablets)
Day 2	600 mg orally (2 × 300 mg tablets)
	Dosage of YEZTUGO: Continuation
Q6M (Q26W) <sup>c</sup> ±2 weeks	927 mg by SC injection (2 × 1.5 mL injections)

<sup>a</sup>Dosing schedule for initiation and continuation in adults and adolescents weighing ≥35 kg; <sup>b</sup>The complete initiation dosing schedule, consisting of SC injections and oral tablets, is required. The efficacy of YEZTUGO has only been established with this dosing schedule; °From date of last injection

Q6M, every 6 months; Q26W, every 26 weeks

Approved for Use on 18 Aug 2025



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#### 2.3 Recommended Dosage

The YEZTUGO dosing schedule in adults and adolescents weighing at least 35 lg consists of a required initiation dosing (subcutaneous injections and oral tablets) followed by once every 6-months continuation dosing (subculaneous injections) (Table 1), YEZTUGO oral tablets may be taken with or without food Dosing Schedule for YEZTUGO Initiation and Continuation in Adults [see Clinical Pharmacology (12.3)].

Dosage of YEZTUGO: Initiation*  Dosage of YEZTUGO: Initiation*  927 mg by subcutaneous injection (2 x 1,5 mL injections)  and and another and another initiation (2 x 1,5 mL injections)
927 mg by subcutaneous 1,1 and and an tablets)
600 mg orally (2 x 300 mg
600 mg orally (2 x continuation
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2.4 Dosing Schedule for Missea

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#### **QUESTION 1**

The indicated dosage for YEZTUGO is 927 mg by 2 x 1.5 mL SC injections and 600 mg orally on Day 1; 600 mg orally on Day 2; and 927 mg by 2 x 1.5 mL SC injections every 6 months thereafter

TRUE (OR) FALSE



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Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2), and

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nts Weighing at Least 35 kg

	Dosage of YEZTUGO: Initiation*  927 mg by subculaneous injection (2 x 1.5 mL injectors)  and on publies)
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	and by subcutaneous and
	927 mg by sacro
Day 1	000 mg grally (2 x 300 mg Usto)
Day	600 mg 430les
	600 mg orally (2 x 300 mg tablets) 600 mg orally (2 x 300 mg tablets) Dosage of YEZTUGO: Continuation
22	Dosage of the control
Day 2	2 x 15 mL metalin
	and by Subcutal local
Every	Dosage on To Dosag
6-months	subcutaneous injection schedule
oc weeks)	ensisting of succeed with this use
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+/-2 West initiatio	n dosing Ligo has only
The complete intention required; the efficacy required; the efficacy From the date of the	927 mg by subcutaneous rejection in obtaing schedule, consisting of subcutaneous reactors are on tables. of TETUCO has only been established with ten desiring schedule. last rejection.
The Contract the efficact	Leet injection.

If the Day 2 oral initiation dose (600 mg, see Table 1) is missed, take it as soon as specially not take the flam of the flam If the Uay Z oral initiation dose (600 mg, see Table 1) is missed, take it as so, possible. Do not take Day 1 and Day 2 oral initiation doses on the same day.

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TRUE. Please refer to section 2.3 of the USPI for further information



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Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2), and Microbiology (12.4)].

#### 2.3 Recommended Dosage

The YEZTUGO dosing schedule in adults and adolescents weighing at least 35 kg consists of a required initiation dosing (subcutaneous injections and oral tablets) followed by once every 6-months continuation dosing (subcutaneous injections) (Table 1). YEZTUGO oral tablets may be taken with or without food [see Clinical Pharmacology (12.3)]. Dosing Schedule for YEZTUGO Initiation and Continuation in Adults

$\overline{}$	Dosage of YEZTUGO: Initi	ation ( miections)
Time	Dosage injection (2 x	1.5 III. 34
	927 mg by subcutaries and	(1.44)
- 1		
Day 1	600 mg orany (2 300 mg	ablets)
1	600 mg orally (2 x 300 mg 600 mg orally (2 x 300 mg Dosage of YEZTUGO: Cont	inuation
Day 2	Dosage v.	- ( injections)
	ination (2)	x 1.5 mL injects
	Dosage of 12.  927 mg by subcutaneous injection (2.	Links
Every	927 mg by sub-	stone and oral tables
s months	horitaneous in	dosing schedule.
oc weeks)	to consisting of succeed with the	000-0
1/2 weeks	docing schedule, only been estaurant	
-lote initiation	VEZTUGO has die	
The complete efficacy	927 mg by subcutaneous injection in in dosing schedule, consisting of subcutaneous it of YEZTUCO has only been established with this last rejection.	
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2.4 Dosing Schedule for Misse

If the Day 2 oral initiation dose (600 mg, see Table 1) is missed, take it as soon as need to be some day or and initiation doses on the same day needlike Day 1 and Day 2 oral initiation doses on the same day. If the Day 2 oral initiation dose (600 mg, see Table 1) is missed, take it as so, the Day 2 oral initiation doses on the same day. Possible. Do not take Day 1 and Day 2 oral initiation doses on the same day. During continuation dosing, if the scheduled 6-month injection is anticrated to be some continuation dosing, if the scheduled 6-month injection is anticrated to be desired to the dosing delayed by more than 2 weeks. YEZTUGO tablets may be taken on an interm basis for the dosing delayed by more than 2 weeks. YEZTUGO tablets may be to Table 2 below for the dosing up to 6 months it needed), until injections resume. Refer to Table 2 below for the dosing up to 6 months it needed), until injections resume.

**QUESTION 2** 

This dose is indicated in adults and adolescents weighing ≥25 kg

TRUE (OR) FALSE



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Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2), and Microbiology (12.4)].

#### 2.3 Recommended Dosage

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Time	Dosage of YEZTUGO: Initiation*  Dosage of YEZTUGO: Initiation*  927 mg by subroutaneous rejection (2 x 1.5 ml. rijectoris)  and  and  and  and  and  and  and  an
	927 mg by subcutaneous "194" and and subplets)
Day 1	600 mg orally (2 x 300 mg
	600 mg orally (2 x 300 mg tablets) 600 mg orally (2 x 300 mg tablets) Dosage of YEZTUGO: Continuation
22	
Day 2	- sm /2 x 1.5 mL injection
EvelV	977 mg by subcutaneous "3
6-months	of subcutaneous injections achedule.
(26 weeks)	erhedule, consisting of stablished with the
+/-2 Webs	927 mg by subcutaneous rejection in or dozing schedule, consisting of subcutaneous rejections and oral tabels, a no foreign schedule, consisting of subcutaneous rejections and oral tabels, a not NEZT LIGO has only been established with this disense schedule last rejection.
a. The complete incach required; the efficach required; the date of the	last injection.
From the date of	u and Dose

2.4 Dosing Schedule for Missed Dos If the Day 2 oral initiation dose (600 mg, see Table 1) is missed, take 1 as soon as needed to the came day of the Day 2 oral initiation doses on the came day of the Day 1 and Day 2 oral initiation doses on the came day

**QUESTION 2** 

This dose is indicated in adults and adolescents weighing ≥25 kg



FALSE. This dose is indicated in adults and adolescents weighing ≥35 kg

Please refer to section 2.3 of the USPI for further information



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Dosage and Administration (2.1), Warnings and Precautions (5.1, 5.2), and Microbiology (12.4)].

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Dosing Schedule for YEZTUGO Initiation and Continuation in Adults d Adolescents Weighing at Least 35 kg

Dosing Schedule for Missed Dose

and Addition	Dos	sage of YEZTUGO: Init	ation*	1 1	
Time	- hu ent	cutaneous injection (		-	7
Day 1	600	mg orally (2 x 300 mg	tablets)		
	60 Dos	age of YELTOOL	50.0		
Day 2		indian (2	x 1.5 mL injections)		

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### 2. Dosage and Administration

#### 2.4 Missed Oral Initiation Dose



If the Day 2 oral initiation dose (600 mg; see **Table 1**) is missed:



Take it as soon as possible. Do not take Day 1 and Day 2 oral initiation doses on the same day.

### 2.4 Anticipated Delayed Injections



During continuation dosing, if the scheduled 6-month injection is anticipated to be delayed by more than 2 weeks:



Oral dosing of YEZTUGO tablets may be taken on an interim basis (300 mg Q7D, for up to 6 months if needed), until injections resume. Continuation injection dosage should be resumed within 7 days after the last oral dose.

Q7D, every 7 days



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Table 2.

Time since Last Injection

26 to 28 weeks

Dosing Schedule for Anticipated Delayed Injections: Weekly Oral

last oral dose.

Individuals who miss a scheduled injection visit should be clinically reasss. navaruation what this is surrounced injection who should be uniformly reassessed to ensure resumption of YEZTUGO remains appropriate and that the individual remains HIV-1 negative. During continuation dosing, if more than 28 weeks have elapost since the first translation dosing, if more than 28 weeks have elapost since the first translation.

Dosing Schedule after Missed Injections

the last injection and YEZTUGO tablets have not been taken, see Table 3 below for the dosing schedule after missed injections. Adherence to the injection dosing schedule after missed injections. dosing screedule after missed injections. Adherence to the injection dosing schedule is strongly recommended [see Dosage and Administration (2.2) and Microbiology (12.4)].

Supporemental doses of YEZTUGO are recommended for individuals inflating thera, with either strong CYP3A induces (see Table 4) or moderate CYP3A induces (see Table 4)

Strong CYP3A inducers may be initiated starting at least 2 days after YEZTUGO is the initiated, while moderate CYP3A inducers may be started any time after YEZTUGO is finitiated, while moderate CYP3A inducers may be started any time after YEZTUGO is finitiated.

with either strong CYF3A inducers (see Table 4) or moderate CYF9A inc.
Table 5) [see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]. Strong CYP3A inducers may be initiated starting at least 2 days after YEZTUGO is first unitable mondarate CYP3A inclurers may be started any time after YEZTUGO is initiated.

a. Use on an interim basis only (for up to 6 months if needed).

Oral dosage of 300 mg taken once every 7 days.

Resume the continuation injection dosage within 7 days after the

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#### 2.4 Missed Injections



Individuals who miss a scheduled injection visit should be clinically reassessed to ensure that the individual remains HIV-1 negative and resumption of YEZTUGO remains appropriate.

During continuation dosing, if more than 28 weeks have elapsed since the last injection and YEZTUGO tablets have not been taken:



Reinitiate with initiation dosing schedule from Day 1 (**Table 1**) and then continue with continuation injection dosing.

[see Dosage and Administration (2.2) and Microbiology (12.4)]



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### Dosing Schedule for Anticipated Delayed Injections: Weekly Oral

Last Injection	Dosage of YEZTUGO
Time since Last Injection 26 to 28 weeks	Dosage of TELFOOD  Oral dosage of 300 mg taken once every 7 days.*  Resume the continuation injection dosage within 7 days after the last oral dose.  ———————————————————————————————————

a. Use on an interim basis only (for up to t.

Individuals who miss a scheduled injection visit should be clinically reassess ensure resumption of YEZTUGO remains appropriate and that the individual remains HIV-1 negative. During continuation dosing, if more than 28 weeks have elegoed since the last injection and YEZTUGO tablets have not been taken, see Table 3 below for the one rask injection and 1EZTUGO tables have not been taken, see rable 3 behindlift of dosing schedule after missed injections. Adherence to the injection dosing schedule after missed injections. gosing schedule after missed injections, agrierence to the injection gosing schedule's strongly recommended [see Dosage and Administration (2.2) and Microbiology (12.4)]. Dosing Schedule after Missed Injections

Table 3.	Dosing	Dosage of YEZ	tration dosing schedule	dosing
Timo since	Last Injection	Dosage of TLL:  Reinitiate with initien continue with	h continuation 19	senderate
More than	28 weeks	theritan	in with Str	ong or Moderate

Strong CYP3A inducers may be initiated starting at least 2 days after YEZTUGO is first windown whole mondacrate CYP3A inclurees may be started any time after YEZTUGO is Strong CYP3A inducers may be initiated starting at least 2 days after YEZTUGO is finitiated. While moderate CYP3A inducers may be started any time after YEZTUGO is first indirected.

2.5 Dosage Modifications for Co-administration with Strong or Moderate **CYP3A Inducers** 



Supplemental doses of YEZTUGO are recommended for individuals initiating therapy with either strong or moderate CYP3A inducers (Table 4 and Table 5).

[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]



Strong CYP3A inducers may be initiated starting at least 2 days after YEZTUGO is first initiated



Moderate CYP3A inducers may be started any time after YEZTUGO is first initiated

CYP3A, cytochrome (P450) 3A



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2.6 Preparation and Administration of Subcutaneous Injection

particulate matter and discoloration prior to administration. YEZTUGO injection is a

yellow solution. Do not use YEZTUGO injection if the solution is discolared or if it contains particulate matter. Once the solution is withdrawn from the vals, the

Subcutaneous injections should be administered as soon as possible (see How

Figure 1 identifies the components for use in the administration steps for the withdrawal regule: a nucleumes use components or use in the administration steps for the windown needle injection kit, and the administration steps are provided in Figure 2. The 18-gauge

The injection kit components are for single use only. Two 1.5 mL injections are require.

Warnings and Precautions (5.4)].

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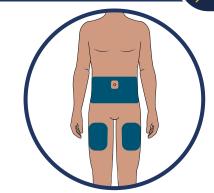
YEZTUGO injection is only for subcutaneous administration into the abdomen by a healthcare provider. The thigh can be used as an alternative injection site if preferred. Do NOT administer intradermally due to risk of serious injection site reactions (see 2.6 Preparation and Administration of Subcutaneous Injection Use a septic technique. Visually inspect the solution in the vials and prepared syringe

> YEZTUGO injection is only for SC administration into the **abdomen** by a healthcare provider. The thigh can be used as an alternative injection site if preferred. Do NOT administer intradermally due to risk of serious ISRs.

[see Warnings and Precautions (5.4)]

Use aseptic technique. Visually inspect the solution in the vials and prepared syringe for particulate matter and discoloration prior to administration. YEZTUGO injection is a yellow solution. Do not use YEZTUGO injection if the solution is discolored or if it contains particulate matter. Once the solution is withdrawn from the vials, the SC injections should be administered as soon as possible.

[see How Supplied/Storage and Handling (16)]





ISR, injection-site reaction



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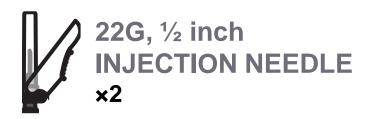
#### Figure 1 > YEZTUGO Withdrawal Needle Injection Kit Components



**Figure 1** identifies the components for use in the administration steps for the withdrawal needle injection kit, and the administration steps are provided in **Figure 2** (next slide). The 18-gauge needle is for withdrawal only in this kit. Two 1.5 mL injections are required for a complete dose.



18G, 1½ inch
WITHDRAWAL NEEDLE
×2



**NOTE:** All components are for single use.

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Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

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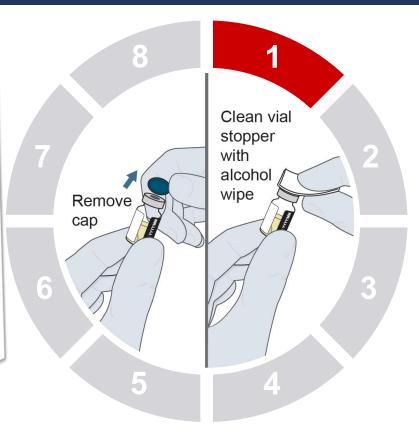
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Figure 2 > YEZTUGO Injection Steps for Withdrawal Needle Injection Kit





1. Prepare vial



Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

Figure 2 YEZTUGO Injection Steps for Withdrawal Needle Injection Kit

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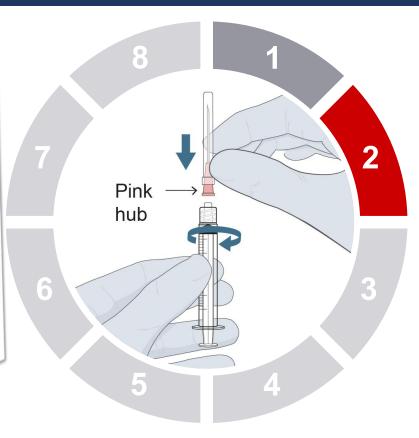
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### Figure 2 > YEZTUGO Injection Steps for Withdrawal Needle Injection Kit





- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe

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Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

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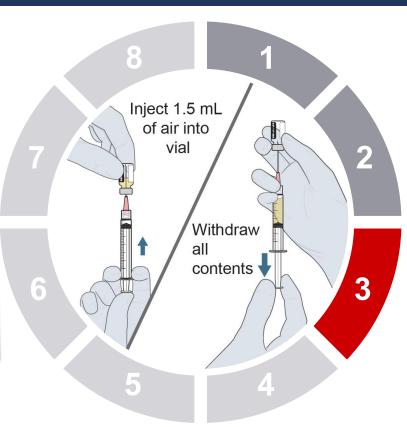
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### Figure 2 > YEZTUGO Injection Steps for Withdrawal Needle Injection Kit





- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe
- 3. Fill syringe



Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

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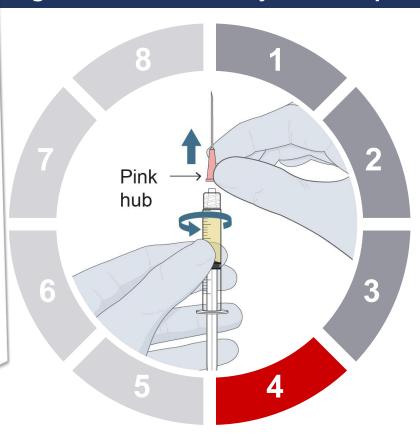
Drug Interactions

Use in Specific Populations

Clinical Studies







- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe
- 3. Fill syringe
- 4. Remove 18G withdrawal needle from syringe

BACK (n) NEXT

Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

Indications & Usage

Dosage & Administration

> Contraindications

Warnings & Precautions

Adverse Reactions

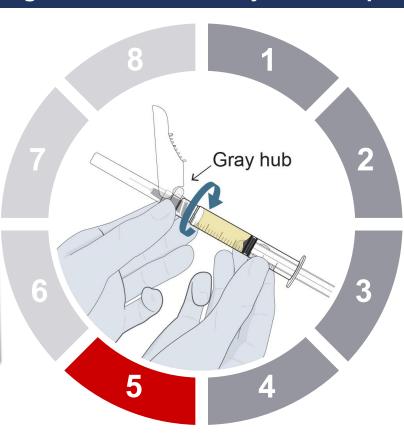
Drug Interactions

Use in Specific Populations

Clinical Studies

#### Figure 2 > YEZTUGO Injection Steps for Withdrawal Needle Injection Kit





- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe
- 3. Fill syringe
- 4. Remove 18G withdrawal needle from syringe
- Attach 22G injection needle to syringe, expel air bubbles, and prime to 1.5 mL



Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

Indications & Usage

Dosage & Administration

Contraindications

Warnings & Precautions

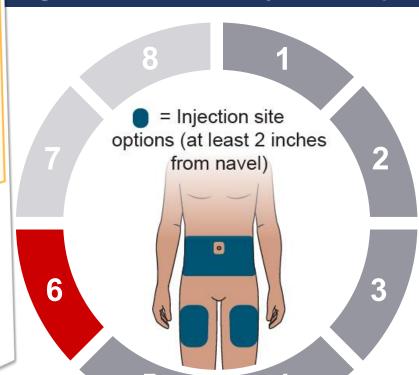
> Adverse Reactions

Drug Interactions

Use in Specific Populations

Clinical Studies

#### Figure 2 > YEZTUGO Injection Steps for Withdrawal Needle Injection Kit



- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe
- 3. Fill syringe
- 4. Remove 18G withdrawal needle from syringe
- Attach 22G injection needle to syringe, expel air bubbles, and prime to 1.5 mL
- 6. Select and clean an injection site



Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

Indications & Usage

Dosage & Administration

Contraindications

Warnings & Precautions

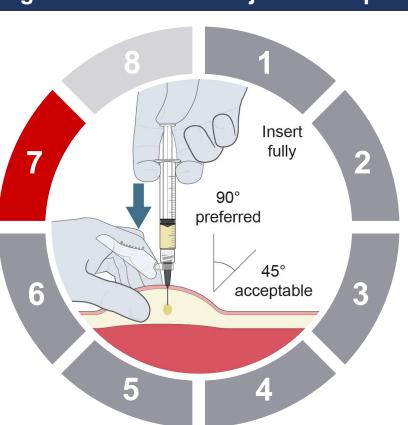
Adverse Reactions

Drug Interactions

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Clinical Studies

#### Figure 2 > YEZTUGO Injection Steps for Withdrawal Needle Injection Kit



- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe
- 3. Fill syringe
- 4. Remove 18G withdrawal needle from syringe
- 5. Attach 22G injection needle to syringe, expel air bubbles, and prime to 1.5 mL
- 6. Select and clean an injection site
- 7. Inject 1.5 mL of YEZTUGO subcutaneously (needle angle to skin: 45–90°, 90° preferred)



Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

Indications & Usage

Dosage & Administration

Contraindications

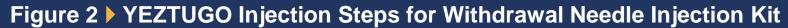
Warnings & Precautions

Adverse Reactions

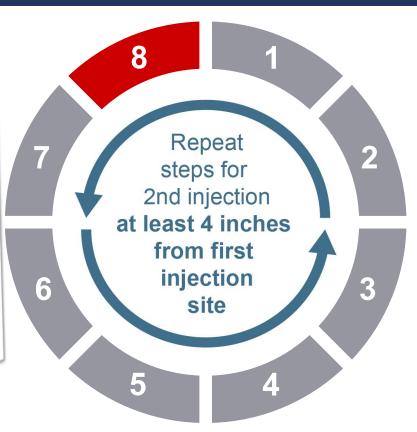
Drug Interactions

Use in Specific Populations

Clinical Studies







- 1. Prepare vial
- 2. Attach 18G withdrawal needle to syringe
- 3. Fill syringe
- 4. Remove 18G withdrawal needle from syringe
- 5. Attach 22G injection needle to syringe, expel air bubbles, and prime to 1.5 mL
- 6. Select and clean an injection site
- 7. Inject 1.5 mL of YEZTUGO subcutaneously (needle angle to skin: 45–90°, 90° preferred)
- **8.** Administer second injection



Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

Indications & Usage

Dosage & Administration

Contraindications

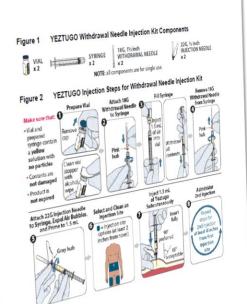
Warnings & Precautions

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**QUESTION 1** 

YEZTUGO should be injected into the subcutaneous space at a 45–90° angle (preferably 90°)

TRUE (OR) FALSE



Indications & Usage

Dosage & Administration

Contraindications

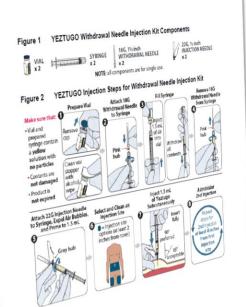
Warnings & Precautions

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#### **QUESTION 1**

YEZTUGO should be injected into the subcutaneous space at a 45–90° angle (preferably 90°)



**TRUE**. YEZTUGO injection is only for **SC** administration into the abdomen by a healthcare provider, and a **90-degree** angle is preferred. The thigh can be used as an alternative injection site if preferred. Do **NOT** administer intradermally due to risk of serious ISRs

Please refer to section 2.6 of the USPI for further information



Indications & Usage

Dosage & Administration

Contraindications

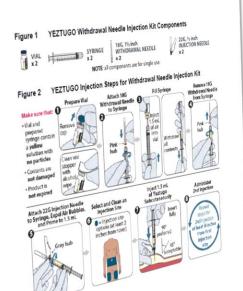
Warnings & Precautions

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**QUESTION 2** 

Two different needles are provided in the YEZTUGO kit. One is for withdrawal and one is for injection

TRUE OR FALSE



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Dosage & Administration

> Contraindications

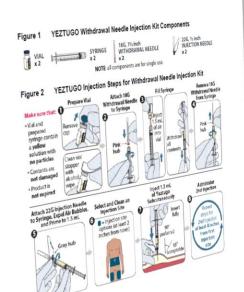
Warnings & Precautions

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#### **QUESTION 2**

Two different needles are provided in the YEZTUGO kit. One is for withdrawal and one is for injection



TRUE. The 18-gauge needle is used for withdrawal and a 22-gauge needle is used for injection

Please refer to section 2.6 of the USPI for further information



# 4. Contraindications

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Dosage & Administration

Contraindications

Warnings & **Precautions** 

> Adverse Reactions

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#### DOSAGE FORMS AND STRENGTHS

YEZTUGO tablets: Each tablet contains 300 mg of lenacapavir (present as 306,8 mg of lenacapavir sodium). The tablets are beige, capsule-shaped, film-coaled, and debossed with 'GSI' on one side of the tablet and '62L' on the other side of the tablet.

YEZTUGO injection: Each single-dose vial contains 463.5 mg/1.5 mL (309 mg/mL) of lenacapavir (present as 473.1 mg/1.5 mL of lenacapavir sodium). The lenacapavir injectable solution is sterile, preservative-free, clear, and yellow with no visible particles.

4 CONTRAINDICATIONS

YEZTUGO is contraindicated in individuals with unknown or positive HIV-1 status feet Warnings and Precautions (5.1)].

5 WARNINGS AND PRECAUTIONS

Comprehensive Management to Reduce the Risk of HIV-1 Infection and Other Sexually Acquired Infections

Use YEZTUGO to reduce the risk of HIV-1 acquisition as part of a comprehensive Use YEZTUGO to reduce the risk of HIV-1 acquigition as part of a comprehensive prevention strategy including adherence to the administration schedule and safet sex prevention strategy including adherence to the administration schedule and safet sex prevention including adherence to the administration schedule and safet sex prevention including adherence to the administration schedule and safet sex prevention including a sex prevention including a sex prevention in the safet prevention strategy including adherence to the administration schedule and safe's support of the providing condoms, to reduce the risk of sexually transmitted infections (CTIE.) VETTI UNIT is not absence affection in representing HIV-1 acquisition (see Clinical Including CTIE.) VETTI UNIT is not absence affections in representing HIV-1 acquisition (see Clinical Including CTIE.) VETTI UNIT is not absence affections in representing HIV-1 acquisition (see Clinical Including CTIE.) VETTI UNIT is not absence affections in representing HIV-1 acquisition (see Clinical Including CTIE.) practices, including condoms, to reduce the risk of sexually transmitted infections (STIs), YEZTUGO is not always effective in prevening HIV-1 acquisition (See Clinical Studies (HI)). The time from initiation of YEZTUGO for HIV-1 PrEP to maximal studies (HI). The time from initiation of YEZTUGO for HIV-1 preP to maximal studies are not reconstructed in a present transfer in inferior is unknown.

Risk for HIV-1 acquisition includes behavioral, biological, or epidemiologic factors including, but not limited to, condomitees sex, past or current STIs, self-identified HIV-1 including, but not limited to, condomitees sex, past or current strains or sexual activity in a biodiction of the sex of sexual activity in a biodiction of the sexual activity in a biodiction

including, but not limited to, condomless sex, past or current \$TIs, self-identified HIV nisk, 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 measures (e.g. correisters and state of the prevention measures) (e.g. correct condom use, knowledge of partner(s) HIV-1 status, including viral sundainables correct condom use, knowledge of partner(s) HIV-1 transmission), inform admirals correct condom uses, knowledge of partner(s) HIV-1 status, including a second partner of the partner of th status; regular testing for STIS that can facilitate HIV-1 transmission). Inform animia about and support their efforts in reducing sexual behaviors associated with HIV-1 about and support their efforts in reducing sexual behaviors associated with HIV-1 about and support their efforts in reducing sexual behaviors associated with HIV-1 about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about and support their efforts in reducing sexual behaviors associated with HIV-1 about and support their efforts in reducing sexual behaviors associated with HIV-1 about and support their efforts in reducing sexual behaviors associated with HIV-1 about and support their efforts in reducing sexual behaviors associated with HIV-1 about an about a support a support a support a support a support

#### 4 Contraindications

YEZTUGO is contraindicated in individuals:



With unknown or positive HIV-1 status.

[see Warnings and Precautions (5.1)]



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Dosage & Administration

> Contraindications

Warnings & **Precautions** 

> Adverse Reactions

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#### DOSAGE FORMS AND STRENGTHS

YEZTUGO tablets: Each tablet contains 300 mg of lenacapavir (present as 306.8 mg of lenacapavir sodium). The tablets are beige, capsule-shaped, film-coated, and debossed with 'GSI' on one side of the tablet and '62L' on the other side of the tablet.

YEZTUGO injection: Each single-dose vial contains 463.5 mg/1,5 mL (309 mg/mL) of lenacapavir (present as 473.1 mg/1.5 mL of lenacapavir sodium). The lenacapavir injectable solution is sterile, preservative-free, clear, and yellow with no visible particles.

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

Warnings and Precautions (5.1)].

- WARNINGS AND PRECAUTIONS
- Comprehensive Management to Reduce the Risk of HIV-1 Infection and Other Sexually Acquired Infections

#### 5.1 Comprehensive Management to Reduce the Risk of HIV-1 Infection and Other Sexually Acquired Infections



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<sup>a</sup> to reduce the risk of STIs. YEZTUGO is not always effective in preventing HIV-1 acquisition.<sup>b</sup> [see Clinical Studies (14)]



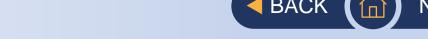
Counsel individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner(s)' HIV-1 status, including viral suppression status; regular testing for STIs that can facilitate HIV-1 transmission). Inform individuals about and support their efforts in reducing sexual behaviors associated with HIV-1 acquisition risk.



Counsel and support individuals on adhering to the YEZTUGO administration schedule, on the use of other measures to reduce the risk of STIs and on the importance of routine testing for HIV-1 and other STIs.

<sup>a</sup>Including condoms; <sup>b</sup>The time from initiation of YEZTUGO for HIV-1 PrEP to maximal protection against HIV-1 infection is unknown

STI, sexually transmitted infection



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# 5. Warnings and Precautions

#### 5.2 Potential Risk of Resistance with YEZTUGO



There is a potential risk of developing resistance to YEZTUGO if an individual acquires HIV-1 either before or when receiving YEZTUGO, or following discontinuation of YEZTUGO. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only YEZTUGO, because YEZTUGO alone does not constitute a complete regimen for HIV-1 treatment. [see Microbiology (12.4)] Test before each injection and additionally as clinically appropriate to confirm HIV-1 negative status.

#### **5.3** Long-Acting Properties and Potential Associated Risks



Healthcare providers should take the long-acting properties of YEZTUGO into consideration when YEZTUGO is prescribed. Residual concentrations of LEN may remain in the systemic circulation of individuals for prolonged periods (up to 12 months or longer after the last SC dose).

It is important to select individuals who agree to the required injection dosing schedule because nonadherence to Q6M injections or missed doses could lead to HIV-1 acquisition and development of resistance.

Q6M, every 6 months

infection are present) using a test approved or cleared by the FDA for the diagnosis of

Counsel and support individuals on adhering to the YEZTUGO administration schedule,

There is a potential risk of developing resistance to YEZTUGO if an individual acquires

HIV-1 infection who are taking only YEZTUGO, because YEZTUGO alone does not Constitute a complete regimen for HIV-1 treatment [see Microbiology (12.4]].

HIV-1 either before or when receiving YEZTUGO, or following discontinuation of YEZTUGO HIV-1 resistance substitutions may emerge in individuals with undiagnosed

negative status using a test approved or cleared by the FDA for the diagnosis or primary HIV-1 infection. Individuals who are confirmed to have HIV-1 must or primary HTV-1 insection. Individuals who are continued to have HtV-1 must immediately begin a Complete HTV-1 treatment regimen to reduce the risk of developing immediately begin a Complete HTV-1 treatment regimen to reduce the risk of developing immediately.

on the use of other measures to reduce the risk of STIs, and on the importance of routine testing for HIV-1 and other STIs. Some individuals, such as adolescents, may benefit from additional counseling and appointment reminders to support adherence to the dosing and testing schedule [see Use in Specific Populations (8.4)].

acute or primary HIV-1 infection [see Dosage and Administration (2.1)].

5.2 Potential Risk of Resistance with YEZTUGO



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Warnings & **Precautions** 

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### 5.4 Serious Injection Site Reactions with Improper Administration

Improper administration (intradermal injection) of lenacapavir has been associated with serious injection site reactions, including necrosis and ulcer. Ensure YEZTUGO is only administered subcutaneously [see Dosage and Administration (2.6)].

#### ADVERSE REACTIONS

The following adverse reactions are discussed in other sections of the labeling:

 Serious Injection Site Reactions with Improper Administration (see Warnings and Precautions (5.4)].

Because clinical trials are conducted under widely varying conditions, adverse reaction because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the rates ouserveu in the clinical trials of a drug cannot be directly compared to rate.
Clinical trials of another drug and may not reflect the rates observed in practice.

The primary safety assessment of YEZTUGO is based on data from two randomized. double-blind, active-controlled trials, PURPOSE 1 and PURPOSE 2 in which a total of the blind, active-controlled trials, PURPOSE 1 and PURPOSE 2. wouse-unity, active-controlled thats, YUKFUSE 1 and FURFOSE 2, in which a tok.

86 16 adult and adolescent participants received YEZTUGO (N=423), DESCOVY oo ro auusi amu aigoiescent pariicipanis received TEZ LUSU (N=5325), UESCOYY

'emitriciabine (FTC)tenofowr alafenamide (TAF), N=2 (35) once daily, of TRUADA

"emitriciabine (FTC)tenofowr alafenamide (TAF), N=2 (35) once daily, of TRUADA terminchaonne (F. Luyrenorovir alasenaminoe (1AF), N=2133) once daily for HW.1 PrEP, In (F.TO/benofovir disoproxil fumarate (TDF), N=2133) once daily for HW.1 PrEP, In IT I Ulternoluvir alsogrami iumarate (IUF; N=2188) once daily for HV: FYEP, M
PURPOSE 1, the median duration of exposure to YETTUGO, DESCOY, and PURPOSE 1, the median duration of exposure to YEZTUGO, DESCOW, and TRUVADA was 43, 42, and 41 weeks, respectively. In PURPOSE 2, the median duration of exposure to have YEZTUGO and TOI IVADA was 90 weeks from the purpose to have YEZTUGO and TOI IVADA was 90 weeks. IRUVAUA was 43, 42, and 41 weeks, respectively. In EURYOSE 2, to. duration of exposure to both YEZTUGO and TRUVADA was 39 weeks.

causality). In PURPOSE 2, 1% of participants in the group receiving YETUGO a

1% of participants receiving TRUVADA discontinued due to adverse events (all

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**5.4** Serious Injection-Site Reactions With Improper Administration



Improper administration (intradermal injection) of LEN has been associated with serious **ISRs**, including necrosis and ulcer. Ensure YEZTUGO is only administered subcutaneously.

[see Dosage and Administration (2.6)]



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infection are present) using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection [see Dosage and Administration (2.1)].

Counsel and support individuals on adhering to the YEZTUGO administration schedule, on the use of other measures to reduce the risk of STIs, and on the importance of routine testing for HIV-1 and other STIs. Some individuals, such as adolescents, may benefit from additional counseling and appointment reminders to support adherence to the dosing and testing schedule [see Use in Specific Populations (8.4)].

### 5.2 Potential Risk of Resistance with YEZTUGO

There is a potential risk of developing resistance to YEZTUGO if an individual acquires There is a potential task of developing resistance to TECTUSU if an inormalial act HIV-1 either before or when receiving YEZTUGO, or following discontinuation of YEZTUGO, HIV-1 resistance substitutions may energe in individuals with undiagnosed HV-1 infection who are taking only YEZTUGO, because YEZTUGO alone does not EHY-1 BITCHOUT WITH OFF LAKING WINY TELLIUSU, DECAUSE TELLIUSU JAIONE OL.

CONSTITUTE a Compilete regimen for HIV-1 treatment [see Microbiology (12.4)].

To minimize this risk, it is essential to test before each injection and additionally as Of transmice uses risk, it is essential to rest perior each injection and additionally as clinically appropriate (e.g., upon diagnosis of other sexually transmitted infections of its properties of the control of the cunicary appropriate (e.g., upon diagnosis of other sexually transmitted infections or is clinical symptoms consistent with acute HIV-1 infection are present to confirm HIV-1. cinical symptoms consistent with a cure HiV-1 intection are present to contine HiV-1 negative status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the FDA for the diagnosis of acute the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared by the status using a test approved or cleared b negative status using a test approved or cleared by the FDA for the diagnosis or primary HIV-1 infection. Individuals who are confirmed to have HIV-1 must or primary HIV-1 infection. Individuals who are confirmed to have HIV-1 must immediately begin a complete HIV-1 treatment regimen to reduce the risk of developing resistance.

In addition, due to the long-acting properties of YEZTUGO, atternative forms of PFEP should be conscienced following discontinuation of YEZTUGO for those individuals with

In addition, due to the long-acting properties of YEZTUGO, alternative forms of PFEP should be considered following discontinuation of YEZTUGO for those individuals with Should be considered following discontinuation of YEZTUGO for those individuals with NATURE and Action and Individuals with AMPU-1 near-attion deather within are at construction risk of LIV.1 accordance and instant within are at construction risk of LIV.1 accordance and instant within are at construction risk of LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and instant within a construction of the LIV.1 accordance and the LIV.1 accordance Should be considered following discontinuation of YEZTUGG for those individuals with HIV-1 negative status who are at continuing risk of HIV-1 acquisition and initiated within 30 weeks of the last YEZTUGG intection (see Warnings and Precautions (5.3)). HIV-1 negative status who are at continuing risk of HIV-1 acquisition and initiate.

28 weeks of the last YEZTUGO injection [see Warnings and Precautions (5.3)]. Long-Acting Properties and Potential Associated Risks with YEZTUGO

owders should take the long-acting properties of YEZTUGO into

Healthcare providers should take the long-acting properties of YEZTUGO into consideration when YEZTUGO is prescribed. Residual concentrations of lens represent consideration when YEZTUGO is prescribed. Residual concentration of an environment of the content o consideration when YEZTUGO is prescribed. Residual concentrations of tenarcognic may remain in the systemic circulation of individuals for prolonged periods up to 12 months or former after the last subrustaneous doses. It is important to select individuals who agree to the required injection dosing schedule because non-adherence to every.6-monthly injections or missed doses could lead to be every.6-monthly injections or missed doses could lead to be every.6-monthly injections or missed doses could lead to be every.6-monthly injections or missed doses could lead to be every.6-monthly injections or missed doses could lead to be every.6-monthly injections or missed doses could lead to be every formula to be every formu It is important to select individuals who agree to the required injection dusing schedul.

He cause non-adherence to every 6-monthly injections or missed doses could lead to HV-1 acounsition and development of resistance.

Lenacapavir, a moderate Cyp3A inhibitor, may increase the evigoure to, and thirefore the control of the control

**QUESTION 1** 

YEZTUGO alone does **not** constitute a complete regimen for HIV-1 **treatment** 

TRUE (OR)



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infection are present) using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection [see Dosage and Administration (2.1)].

Counsel and support individuals on adhering to the YEZTUGO administration schedule, on the use of other measures to reduce the risk of STIs, and on the importance of routine testing for HIV-1 and other STIs. Some individuals, such as adolescents, may benefit from additional counseling and appointment reminders to support atherence to the dosing and testing schedule [see Use in Specific Populations (8.4)].

### 5.2 Potential Risk of Resistance with YEZTUGO

There is a potential risk of developing resistance to YEZTUGO if an individual acquires HIV.1 either before or when receiving YEZTUGO, or following discontinuation of YEZTUGO, HIV-1 resistance substitutions may emerge in individuals with undiagnosed HV-1 infection who are taking only YEZTUGO, because YEZTUGO alone does not COnstitute a complete regimen for HIV-1 treatment [see Microbiology (12.4)].

To minimize this risk, it is essential to test before each injection and additionally as U Hamaniace was 1556, 16.20 essential to rest dende each agenor and automorary as of chinically appropriate (e.g., upon diagnosis of other sexually transmitted infectors or the chinically appropriate (e.g., upon diagnosis of other sexually transmitted infectors or the chinically appropriate (e.g., upon diagnosis of other sexually transmitted infectors or the chinically appropriate (e.g., upon diagnosis of other sexually transmitted infectors or the chinically appropriate (e.g., upon diagnosis of other sexually transmitted infectors or the chinically appropriate). currically appropriate (e.g., upon diagnosis of other sexually transmitted infections of a clinical symptoms consistent with acute HIV-1 infection are present to confirm HIV-1 currical symptomics consistent with acure Hiv-1 infection are present to continue Hiv-1 negative Status using a feet approved or cleared by the FDA for the diagnosis of acure negative Status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status using a feet approved or cleared by the FDA for the diagnosis of acure negative status acres negative status negative status using a test approved or cleared by the FUA for the diagnosis to primary HIV-1 infection. Individuals who are confirmed to have HIV-1 must or primary HIV-1 infection. Individuals who are confirmed to have HIV-1 must immediately begin a complete HIV-1 treatment regimen to reduce the risk of developing posietance.

In addition, due to the long-acting properties of YEZTUGO, alternative forms of PEP should be considered following discontinuation of YEZTUGO for those individuals with the should be considered following discontinuation of YEZTUGO for those individuals with the should be considered following discontinuation of YEZTUGO, alternative and interest values of the should be considered following discontinuation of YEZTUGO, alternative forms of PEP should be considered for the should Should be considered following discontinuation of YEZTUGO for those individuals with HIV-1 negative status who are at continuing risk of HIV-1 acquisition and nitiated within Yellow weake of the last YEZTUGO insertion feee Warnings and Presautions (5 3).

HIV-1 negative status who are at continuing risk of HIV-1 acquisition and initiale.

28 weeks of the last YEZTUGO injection [see Warnings and Precautions (5.3)]. Long-Acting Properties and Potential Associated Risks with YEXTUGO

#### **QUESTION 1**

YEZTUGO alone does **not** constitute a complete regimen for HIV-1 **treatment** 



TRUE. Individuals who are confirmed to have HIV-1 must immediately begin a complete HIV-1 treatment regimen to reduce the risk of developing resistance

Please refer to section 5.2 of the USPI for further information



Indications & Usage

Dosage & Administration

> Contraindications

Warnings & **Precautions** 

> Adverse Reactions

Drug Interactions

Use in Specific Populations |

Clinical Studies

#### 5.4 Serious Injection Site Reactions with Improper Administration

Improper administration (intradermal injection) of lenacapavir has been associated with serious injection site reactions, including necrosis and ulcer. Ensure YEZTUGO is only administered subcutaneously [see Dosage and Administration (2.6)].

#### ADVERSE REACTIONS

The following adverse reactions are discussed in other sections of the labeling:

 Serious Injection Site Reactions with Improper Administration [see Warnings and Precautions (5.4)].

Because clinical trials are conducted under widely varying conditions, adverse reaction because cumical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the raises supperved in the comican trials of a drug cannot be directly compared to rate. Clinical trials of another drug and may not reflect the rates observed in practice.

The primary safety assessment of YEZTUGO is based on data from two randomized. obuble-blind, active-controlled trials, PURPOSE 1 and PURPOSE 2, in which a total of outure-turing, active-controlled thats, PURFUSE 1 and PURFUSE 2, in which a bis.

8616 adult and adolescent participants received YEZTUGO (N=423), DESCOVY. 80 TO adult and adolescent participants received YEZTUGO (N=323), DESCOYY (emtricitabine [FTC]/tenofovir alafenamide [TAF], N=2135) once daily, or TRU/ADA (FTC)/tenofovir riseoriroval furniarate TTDE1 N=2150 once daily for HIIV.1 PVEP In (FTC)/tenorirovar riseoriroval furniarate TTDE1 N=2150 once daily for HIIV.1 PVEP In terminicitatione || Lichtenotovir alatenamioe || LAF, N=2135) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily for HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily for HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

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(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF, N=2159) once daily or HW.1 PrEP, in |

(FTO/benotovir disoproxis firmarate || TDF (F1U/tenotowif disoproxil furnarate [TDF]; N=2158) once daily for HIV-1 PFEP. In PURPOSE 1, the median duration of exposure to YEZTUGO, DESCOVY, and TRI IVADIA was 43, 47, and 41 wassic reconstribute in PURPOSE 2 the median TRI IVADIA was 43, 47, and 41 wassic reconstribute. PURFOSE 1, the median duration of exposure to YEZTUGO, DESCOVY, and TRUVADA was 43, 42, and 41 weeks, respectively. In PURFOSE 2, the median truth and the second section of exposure to hostly VEZTUGO and TRUVADA was 39 weeks. TRUVALIA Was 43, 42, and 41 weeks, respectively. In FURPOSE 2, th. duration of exposure to both YEZTUGO and TRUVADA was 39 weeks.

The most common adverse reactions (all Grades) reported in at least 5% of participants receiving YEZTUGO in either PURPOSE 1 or PURPOSE 2 were anjection ste reactions, and no account of the purpose 1 of the purpose 2 were anjection and purpose 1 or pur headache, and nausea. In PURPOSE 1, <1% of participants in the groups received YETUGO, DESCOYY or TRUVADA, discontinued due to adverse events (all YETUGO, DESCOYY or TRUVADA, discontinued due to adverse events (all YETUGO, DESCOYY or TRUVADA discontinued due to adverse events (all YETUGO, DEVENTE CAUSAITY). In PURPOSE 2, 1% of participants in the group receiving a very causality. In PURPOSE 2, 1% of participants receiving TRUVADA discontinued due to adverse events (all YETUGO, DEVENTE CAUSAITY). causainy). In PURPOSE 2, 1% of participants in the group receiving YEZTUGO and a classification of the group receiving YEZTUGO and a classification of the group receiving TRUVADA discontinued due to adverse events (all Grastes) in all last causains and participants receiving TRUVADA discontinued due to adverse events (all Grastes) in a classification of the group of adverse reactions (all Grastes) and last causains and participants received a very received of the group causality). Table 6 presents the frequency of adverse reactions (all Grades) in . 2% of participants receiving YEZTUGO in either PURPOSE 1 or PURPOSE 2.

**QUESTION 2** 

Improper administration (ex. intradermal injection) of LEN has been associated with serious ISRs, including necrosis and ulcer

TRUE (OR) FALSE

ISR, injection-site reaction



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Dosage & Administration

> Contraindications

Warnings & **Precautions** 

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#### 5.4 Serious Injection Site Reactions with Improper Administration

Improper administration (intradermal injection) of lenacapavir has been associated with serious injection site reactions, including necrosis and ulcer. Ensure YEZTUGO is only administered subcutaneously [see Dosage and Administration (2.6)].

#### ADVERSE REACTIONS

The following adverse reactions are discussed in other sections of the labeling:

Precautions (5.4)].

Because clinical trials are conducted under widely varying conditions, adverse reaction because cumical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the raises supperved in the comican trials of a drug cannot be directly compared to rate. Clinical trials of another drug and may not reflect the rates observed in practice.

The primary safety assessment of YEZTUGO is based on data from two randomized. on the billing, active controlled trials, PURPOSE 1 and PURPOSE 2, in which a total of the billing, active controlled trials, PURPOSE 1 and PURPOSE 2, in which a total of the billing, active controlled trials, PURPOSE 1 and PURPOSE 2, in which a total of the billing and the billing active controlled trials. outure-outing, acrove-controlled mals, PURPUSE 1 and PURPUSE 2, in which a tok.

86 16 adult and adolescent participants received YEZTUGO (N=4223), DESCOY ou to assure and adulescent participants received TELLUGU (N=\$33), UESQUY (emtrictabine [TC]) tendrolfolia alafenamide [TAF], N=2135) once daily, or TRUADA (ETT) in accordant of tendrolfolia alafenamide (TAF). N=2150 once daily for all VI type in (ETT) in accordant of tendrolfolia from sendolfolia (TAF). remincitatione [1-1.Cytenorovir alatenamino [1AF], N=2135) once daily or HW.1 PrEP, in FT. Crenofovir disoproxil furnarate [TDF], N=2158) once daily for HW.1 PrEP, in It Tutenotour disoprorii tumarate [TDF], N=2150) once daily for HV-1 PVEP, Is, PVEP, I FURFOSE 1, the median duration of exposure to YEZTUGO, DESCOVY, and TRUVADA was 43, 42, and 41 weeks, respectively. In PURFOSE 2, the median duration of avenuation to host YEZTUGO and TRUVADA was 30 weeks duration of avenuation to hosts. INUVAUA was 43, 42, and 41 weeks, respectively. In PURPOSE 2, th. duration of exposure to both YEZTUGO and TRUVADA was 39 weeks.

<1% of participants receiving TRUVADA discontinued due to adverse events (all causes) at least causality). Table 6 presents the frequency of adverse evactions (all Grades) at least causality). Table 6 presents the frequency of adverse evactions of PURPOSE 1 of PURPOSE 2 and rearticipants reveiving YETTLIGO in either PURPOSE 1 of PURPOSE 2.</p> causality). Table 6 presents the frequency of adverse reactions (all grades) in 2% of participants receiving YEZTUGO in either PURPOSE 1 or PURPOSE 2.

**QUESTION 2** 

Improper administration (ex. intradermal injection) of LEN has been associated with serious ISRs, including necrosis and ulcer



TRUE. Ensure YEZTUGO is only administered subcutaneously

Please refer to sections 5.4 and 2.6 of the USPI for further information

ISR, injection-site reaction



### 6. Adverse Reactions

Indications & Usage

Table 6.

Adverse Reaction

Injection Site

Reactions

Dosage & Administration

> Contraindications

Warnings & Precautions

Adverse Reactions

Drug Interactions

Use in Specific Populations

**Clinical Studies** 

### **6.1** Clinical Trials Experience





The most common adverse reactions (all Grades) reported in ≥5% of participants receiving YEZTUGO in either PURPOSE 1 or PURPOSE 2 were ISRs, headache and nausea.

#### Table 6. Adverse Reactions (All Grades) Reported in ≥2%<sup>b</sup> of Participants Receiving YEZTUGO in PURPOSE 1 and PURPOSE 2

	PURPOSE 1		PURPOS	SE 2
Adverse Reaction	YEZTUGO N=2140	TRUVADA <sup>c</sup> N=1070	YEZTUGO N=2183	TRUVADA <sup>c</sup> N=1088
ISRs	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%

<sup>a</sup>Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice; <sup>b</sup>Frequencies of adverse reactions are based on all AEs attributed to study drug (or to the procedure for ISRs) by the investigator; Participants received placebo SC injections (polyethylene glycol 400);

ISR, injection-site reaction

Adverse Drug Reactions (All Grades) Reported in ≥2% of

TRUVADA<sup>b</sup> N=1088

69%

Participants Receiving YEZTUGO in PURPOSE 1 or

Participants received placebo subcutaneous injections (polyethylene glycol 400).

The most trequent adverse reactions associated with lenacapavir injection for subcustaneous use in PURPOSE 1 and PURPOSE 2 were ISRs. The most commonly subcustaneous use in PURPOSE 1 and PURPOSE 2 were ISRs. The most commonly in the Israel Israel

SUDCUITANEOUS USE IN PUNPFUSE 1 and PURPFUSE 2 were ISRs. The most commons, reported ISRs (all grades) in at least 2% of participants who received YEZTUGO in ather PUNPFUSE 5 or PUNPFUSE 2 are received in Table 7 in the PUNPFUSE 5 or PUNPFUSE 5 are received in Table 7.

ulcer and nodule. YEZTUGO was discontinued due to ISRs in 4 (0.2%) participation of the ISRs were serious. The incidence of reported ISRs decreased with Note of the ISRs were serious.

reported ISMS (all grades) in at least 2% of participants who is either PURPOSE 1 or PURPOSE 2 are presented in Table 7.

Injection-Associated Adverse Reactions

Local Injection Site Reactions (ISRs)

PURPOSE 2

Approved for Use on 18 Aug 2025



## 6. Adverse Reactions

Indications & Usage

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173 (interquartile range: 22, 267) days. The median duration of ISRs, excluding nodules and indurations, was 9 (interquartile range: 4 to 30) days.

In PURPOSE 2, 83% of participants receiving YEZTUGO experienced ISRs, compared to 69% of participants receiving placebo injections (and TRUVADA). Most participants had mild (Grade 1, 66%) or moderate (Grade 2, 17%) severity ISRs. Grade 3 ISRs were reported in 14 (0.6%) participants, and included ulcer, pain, eythema, edema, and dematitis, YEZTUGO was discontinued due to ISRs in 26 (12%) participants. None of the ISRs were serious. The incidence of reported ISRs decreased with subsequent

Nodules: Injection site nodule was reported in 63% of participants who received YEZTUGO and resolved more slowly than other ISRs. The median duration of acute Victorians was required in other ISRs. The median duration of acute Victorians was required in the Victorian other ISRs. TEX LUGU and resorved more slowly man other losts, the median duration of nodules associated with the first injections of YEZTUGO was 287 (interquantle range, 176, 42). associated with the first injections of TEL LUGU was 241 (interquante range, 176, 423) days. The median of the maximum observed nodule diameter for each participant was

Other ISRs: The other ISRs reported in more than 2% of participants who received VINEY NONS, THE OWER TORKS reported in more man 2% or participants who received YEZTUGO were pain (50%), eyythema (17%), induration (16%), swelling (7(%), brusing 17%), induration (16%), swelling (16%), s YEZTUGU were pain (56%), erythema (17%), induration (16%), swelling (7%), b. (3%), pruritus (3%), and warmth (2%). The median duration of induration, which (3%), pruntus (3%), and warmth (2%). The median duration of induration, which resolved more slowly than most other ISRs, was 151 (interquantile range: 15, 67) days.

The median duration of ISRs earthwise and indurations was 4 (interquantile range). resolved more slowly than most other ISRs, was 151 (interquartile range: 15, 267) day. The median duration of ISRs, excluding nodules and indurations, was 4 (interquartile and other lands) of the second of ISRs, excluding nodules and indurations, was 4 (interquartile and other lands).

Site Reactions (All Grades) Reported in 22% of

range. 2 to	Injection Site Reservit	19 YEZTOO	PURPOSE 2
Table 7.	Injection Site Receiving Participants Receiving PURPOSE 2	-110	TRUVALI
	PURFO	N=218	39%
639	YEZTUGO TH	N=3205 65%	10%
Injection Site Reactions	64%	24% 16%	3%
Nodule	31%	5% 3%	19%
Pain Induration	4% 2% 1% < 1% < 1% < 1% < 1% < 1% < 1% <	1% 1%	2% po procedure)
Swelling	1%	<1% 2%	ady drug (or to and
Pruntis Erythema	<1%	ite reactions attribute	e glycol <sup>4007</sup>
Bruising Warmth	es are based on all rijes	eous injections v	13
Via Coopen	-ctig3101 , placebo		

## 6.1 Clinical Trials Experience (continued)

## Table 7. ISRs (All Grades) Reported in ≥2%<sup>b</sup> of Participants Receiving YEZTUGO in PURPOSE 1 or PURPOSE 2

	PURPOSE 1		PURPOSE 2	
ISRs	YEZTUGO N=2140	DESCOVY or TRUVADA <sup>c</sup> N=3205	YEZTUGO N=2183	TRUVADA <sup>c</sup> 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%



### **PURPOSE 1:**

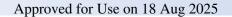
- Grade 3 ISRs were reported in 4 (0.2%) participants
- Included ulcer and nodule

### **PURPOSE 2:**

- · Grade 3 ISRs were reported in 14 (0.6%) participants
- Included ulcer, pain, erythema, edema and dermatitis

<sup>a</sup>Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice; <sup>b</sup>Frequencies are based on all ISRs attributed to study drug (or to the procedure) by the investigator; Participants received placebo SC injections (polyethylene glycol 400)

ISR, injection-site reaction





### Indications & Usage

Nodules and Indurations Dermatopathology

granulomatous response in some participants.

7.1 Effect of Other Drugs on YEZTUGO Lenacapavir is a substrate of P-gp, UGT1A1, and CYP3A.

DRUG INTERACTIONS

In a separate clinical trial (CAPELLA) in participants with HIV-1 who received lenacapavir via subcutaneous injection, skin biopsies of injection site nodules or

indurations revealed dermatopathological findings of foreign body inflammation or

Drugs that are strong or moderate inducers of CYP3A may significantly decrease

plasma concentrations of lenacapavir, which may reduce the effectiveness of

Administration (2.5) and Cirrical Pharmacology (12.3). Combined P-gp, UGT1A1, and Strong CYP3A Inhibitors

these inhibitors is not recommended.

7.2 Effect of YEZTUGO on Other Drugs

YEZTUGO. Therefore, dosage modifications (supplemental doses) of YEZTUGO are recommended when initiating strong or moderate Cyp3A inducers (see Dosage and

Combined P-gp, UGTIA1, and strong CYPA inhibitors may significantly increase placema concentrations of VE7TI I/20 Communities administration of VE7TI I/20 Communities administration of VE7TI I/20 Communities administration

Lenacapavir is a moderate inhibitor of CYP3A and a P-gp inhibitor.

Combined Y-gp, UG 11A1, and strong CYF3A inhibitors may significantly increase plasma concentrations of YEZTUGO concomitant administration of YEZTUGO with these inhibitories is not recommended.

Dosage & Administration

> Contraindications

Warnings & Precautions

> Adverse Reactions

Drug Interactions

Use in Specific Populations

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## 7. Drug Interactions

## 7.1 Effect of Other Drugs on YEZTUGO





LEN is a substrate of P-gp, UGT1A1 and CYP3A.



## **Strong or Moderate CYP3A Inducers**

Drugs that are strong or moderate inducers of CYP3A may significantly decrease plasma concentrations of LEN, which may reduce the effectiveness of YEZTUGO. Therefore, dosage modifications (supplemental doses) of YEZTUGO are recommended when initiating strong or moderate CYP3A inducers.

[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3)]



## Combined P-gp, UGT1A1 and Strong CYP3A Inhibitors

These drugs may significantly increase plasma concentrations of YEZTUGO. Concomitant administration is not recommended.

CYP3A, cytochrome (P450) 3A; P-qp, P-glycoprotein; UGT1A1, UDP-glucuronosyltransferase family 1 member A1



## 7. Drug Interactions

Indications & Usage

Dosage & Administration

> Contraindications

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### Nodules and Indurations Dermatopathology

In a separate clinical trial (CAPELLA) in participants with HIV-1 who received lenacapavir via subcutaneous injection, skin biopsies of injection site nodules or indurations revealed dermatopathological findings of foreign body inflammation or granulomatous response in some participants.

### DRUG INTERACTIONS

## 7.1 Effect of Other Drugs on YEZTUGO

Lenacapavir is a substrate of P-gp, UGT1A1, and CYP3A.

Drugs that are strong or moderate inducers of CYP3A may significantly decrease plasma concentrations of lenacapavir, which may reduce the effectiveness of PRASHINA CONCENHAUDIS ON MEMACABANNI, WINCH may reduce the enecumeness of YEZTUGO. Therefore, dosage modifications (supplemental doses) of YEZTUGO are recommended when initiating strong or moderate CypsA inducers (see Dosage and

Administration (2.5) and Cirrical Pharmacology (12.3).

Combined P-99, UGT1A1, and Strong CYP3A Imbibliors Combined P-gp, UGT1A1, and strong CYP-A inhibitors may significantly increase of the component of the compon Combined P-gp, UGT1A1, and strong CYP3A inhibitors may significantly increase plasma concentrations of YEZTUGO with those inhibitance in role recommended.

these inhibitors is not recommended.

Effect of YEZTUGO on Other Drugs

## 7.2 Fifect of YEZTUGO on Other Drugs

LEN is a moderate inhibitor of CYP3A and a P-gp inhibitor.



The co-administration of YEZTUGO with sensitive substrates of CYP3A or P-gp may increase the concentrations of these substrates and result in the increased risk of their AEs. See the prescribing information of these sensitive substrates for dosing recommendations or appropriate monitoring of safety.



Due to the long half-life of LEN following SC administration, YEZTUGO may increase the exposure of drugs primarily metabolized by CYP3A initiated within 9 months after the last SC dose of YEZTUGO. [see Clinical Pharmacology (12.3)]



### Indications & Usage

7.3 Drugs without Clinically Significant Interactions with YEZTUGO

rosuvastatin, tenofovir alafenamide, and voriconazole. 8 USE IN SPECIFIC POPULATIONS

1-800-258-4263.

Based on drug interaction studies conducted with YEZTUGO, no clinically significant drug interactions have been observed with: atorvastatin, famotidine, playastatin,

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to YEZTUGO during pregnancy. Healthcare provides are encouraged to register individuals by Calling the Antiretroviral Pregnancy Registry (APR) at 2 non 200 and 200.

Available ustal from a randomized, controlled that ("CNC"US") with YELF (USO use during pregnancy have not identified a drug-associated risk for miscarriage, or adverse during pregnancy have not identified a drug-associated risk for miscarriage.

Dosage & Administration

> Contraindications

Warnings & Precautions

> Adverse Reactions

Drug Interactions

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## 7. Drug Interactions

## 7.3 Drugs Without Clinically Significant Interactions With YEZTUGO



interactions have been observed, nor are expected, with:

- Atorvastatin
- **Famotidine**
- Pitavastatin

Voriconazole

Based on drug interaction studies conducted with YEZTUGO, no clinically significant drug

- Rosuvastatin
- Tenofovir alafenamide



## 7. Drug Interactions

Indications & Usage

Dosage & Administration

> Contraindications

Warnings & Precautions

> Adverse Reactions

Drug Interactions

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Nodules and Indurations Dermatopathology

In a separate clinical trial (CAPELLA) in participants with HIV-1 who received lenacapavir via subcutaneous injection, skin biopsies of injection ste nodules or indurations revealed dermatopathological findings of foreign body inflammation or granulomatous response in some participants.

## 7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on YEZTUGO

Lenacapavir is a substrate of P-gp, UGT1A1, and CYP3A.

Drugs that are strong or moderate inducers of CYP3A may significantly decrease plasma concentrations of lenacapavir, which may reduce the effectiveness of Plasma concentrations of renacapavir, which may reduce the enectiveness of YEZTUGO. Therefore, dosage modifications (supplemental doses) of YEZTUGO are 1EZTUGU. THEREIOTE, gasage moanications (supplemental doses) of YEZTUGO are recommended when initiating strong or moderate Cyp3A inducers (see Dosage and Administration of Strong Orlando December 1999 at 1999 and Orlando recommended when missing strong or moderate UT-X Administration (2.5) and Clinical Pharmacology (12.3).

Combined P-gp, UGT1A1, and Strong CYP3A Inhibitors Combined P-gp, UGT141, and strong CYP34 inhibitors may significantly increase plasma concentrations of YEZTUGO with these inhibitors is not recommended these inhibitors is not recommended.

presented concentrations of YEE LUGC these inhibitors is not recommended.

7.2 Effect of YEZTUGO on Other Drugs

Lenacapavir is a moderate inhibitor of CYP3A and a P-gp inhibitor.

The Co-administration of YEZTUGO with sensitive substrates of CYP3A or P-go may not consider the increased risk of the increased risk of the increased risk of the increase the Concentrations of these substrates and result in the increase the concentrations of these substrates and result in the increased risk of the concentrations of these sensitive substrates for ossign and verse events. See the prescribing information of these sensitive substrates for ossign and verse events. increase the concentrations of these substrates and result in the increase and result in the increase

Due to the long half-life of lenacapavir following submaring relative by the state of drugs formation after the last subconneous dose by YEZTUGO may increase the exposure of drugs formation after the last subconneous dose YEZTUGO may increase the exposure of drugs formation after the last subconneous dose YEZTUGO may increase the exposure of drugs formation after the last subconneous dose YEZTUGO.

**QUESTION 1** 

YEZTUGO is a moderate inhibitor of CYP3A and a P-gp inhibitor

TRUE (OR) FALSE

CYP3A, cytochrome (P450) 3A; P-gp, P-glycoprotein



## 7. Drug Interactions

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Clinical Studies

Nodules and Indurations Dermatopathology

In a separate clinical trial (CAPELLA) in participants with HIV-1 who received lenacapavir via subcutaneous injection, skin biopsies of injection ste nodules or indurations revealed dermalopathological findings of foreign body inflammation or granulomatous response in some participants.

## DRUG INTERACTIONS

7.1 Effect of Other Drugs on YEZTUGO

Lenacapavir is a substrate of P-gp, UGT1A1, and CYP3A.

Drugs that are strong or moderate inducers of CYP3A may significantly decrease plasma concentrations of lenacapavir, which may reduce the effectiveness of Plasma concentrations of renacapavir, which may reduce the enectiveness of YEZTUGO. Therefore, dosage modifications (supplemental doses) of YEZTUGO are 1EZTUGU. THEREIOTE, gasage moanications (supplemental doses) of YEZTUGO are recommended when initiating strong or moderate Cyp3A inducers (see Dosage and Administration of Strong Orlando December 1999 at 1999 and Orlando

recommended when missing strong or moderate UT-X Administration (2.5) and Clinical Pharmacology (12.3). Combined P-gp, UGT1A1, and Strong CYP3A Inhibitors

Combined P-gp, UGT141, and strong CYP34 inhibitors may significantly increase plasma concentrations of YEZTUGO Concomitant administration of YEZTUGO with these inhibitors in our server members of the programment of the pro these inhibitors is not recommended.

7.2 Effect of YEZTUGO on Other Drugs

Lenacapavir is a moderate inhibitor of CYP3A and a P-gp inhibitor.

**QUESTION 1** 

YEZTUGO is a moderate inhibitor of CYP3A and a P-gp inhibitor



TRUE. Please refer to section 7.2 of the USPI for further information





## 8. Use in Specific Populations

Indications & Usage

Dosage & Administration

> Contraindications

Warnings & **Precautions** 

Adverse Reactions

Drug Interactions

**Use in Specific Populations** 

Clinical Studies

## 7.3 Drugs without Clinically Significant Interactions with YEZTUGO

Based on drug interaction studies conducted with YEZTUGO, no clinically significant drug interactions have been observed with: atorvastatin, famolidine, pitavastatin, rosuvastatin, tenofovir alafenamide, and voriconazole.

## 8 USE IN SPECIFIC POPULATIONS

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to YETUGO during pregnancy. Healthcare providers are encouraged to register individuals by calling the Antiretroviral Pregnancy Registry (APR) at

## 8.1 Pregnancy

Data from PURPOSE 1 have not identified a drug-associated risk for miscarriage, or adverse maternal or fetal outcomes, when compared to the active control. The rate of major birth defects in YEZTUGO-exposed pregnancies did not exceed the background prevalence rates.a There is an increased risk of HIV-1 transmission from the mother to the child during acute HIV-1 infection. [see Clinical Considerations]

## 8.2 Lactation

LEN is present in human milk and was detected at very low levels in infants who were breastfed by individuals who became pregnant while receiving YEZTUGO. No adverse effects of LEN in breastfed infants have been observed.

## 8.4 Pediatric Use

The safety and effectiveness of YEZTUGO for HIV-1 PrEP in adolescents weighing ≥35 kg who are at risk for HIV-1 acquisition is supported by 2 adequate and well-controlled trials, PURPOSE 1 and PURPOSE 2, that enrolled both adults and adolescents.

[see Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Studies (14)]

<sup>a</sup>The risk estimates are imprecise due to small numbers of exposed pregnancies



## 8. Use in Specific Populations

Indications & Usage

The median lenacapavir concentration in human breast milk to maternal plasma ratio in

participants (n=8) who received YEZTUGO was 0.63 (range: 0.29 to 1.90). The median infant-to-mother plasma ratio for lenacapavir in infants (n=10) who were breastled by individuals receiving YEZTUGO from 0 to less than 13 weeks after delivery was 0.06

The safety and effectiveness of YEZTUGO for HIV-1 PIEP in adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition is supported by 2 adequate and wellcontrolled trials, PURPOSE 1 and PURPOSE 2, that enrolled both adults and

consumed urials, PURPUSE 1 and PURPUSE 2, that enroted both adults and adolescents [see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Pharmacology (12.3),

PURPOSE 1 and PURPOSE 2 enrolled a total of 128 adolescent participants. In the 59 TURFUSE: I also FURFUSE & entoned a total or 120 adorescent participants. In the adolescents who received YEZTUGO, the safety data were comparable to the safety

Subsequent injection of YEZTUGO, and additionally as clinically appropriate, using a

subsequent agreement or the Lucy, and auditionary appropriate is test approved or cleared by the FDA for the diagnosis of acide or original HIV.

test approved or created by the PUA tot the usagrous or acute or printer miner infection. Adolescents may benefit from additional counseling and appointment intection. Adolescents may benefit from adoltonal counseling and appointment reminders to support adherence to the dosing and testing schedule (see Dosage and Administration 7.2.2). Marminne and Diranal Service 15. 11

THE safety, emetaweness, and pharmaconmetes of , weighing less than 35 kg have not been established.

Dosage & Administration

> Contraindications

Warnings & **Precautions** 

> Adverse Reactions

Drug Interactions

**Use in Specific Populations** 

Clinical Studies

## 8.5 Geriatric Use

Clinical studies of YEZTUGO did not include sufficient numbers of participants aged ≥65 years to determine whether they respond differently from younger individuals. Exercise caution when administering YEZTUGO in elderly individuals due to greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy. [see Clinical Pharmacology (12.3)]

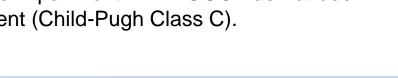
## 8.6 ▶ Renal Impairment

with ESRD (eCrCl <15 mL/min). [see Clinical Pharmacology (12.3)]

No dosage adjustment of YEZTUGO is recommended in individuals with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. YEZTUGO has not been studied in individuals with severe hepatic impairment (Child-Pugh Class C). [see Clinical Pharmacology (12.3)]

No dosage adjustment of YEZTUGO is recommended in individuals with mild, moderate or severe renal impairment (eCrCl ≥15 mL/min). YEZTUGO has not been studied in individuals

## 8.7 Hepatic Impairment



eCrCl, estimated creatinine clearance; ESRD, end-stage renal disease



### Indications & Usage

A treatment-related increase in the incidence of malignant sarcoma at the injection site

was observed in males and a treatment-related increase in combined benign fibroma and malignant fibrosarcoma at the injection site was observed in females, at the highest

dose (927 mg/kg). This dose in rats resulted in an exposure approximately 44 times the

Lenacapavir was not mutagenic in a battlery of in vitro and in vivo genotoxicity assays. Lenacaparar was not munagena, at a usunery or at ord and it was generously assay including microbial munagenesis, chromosome aberration in human peripheral blood

There were no effects on fertility, mating performance or early embryonic developm.

When lenacapavir was administered to rais at systemic exposures (AUC) 8 times the

The efficacy and safety of YEZTUGO in reducing the risk of HIV-1 acquisition were

The emcacy and sarety of YEZIUGU in reducing the risk of HIV-1 acquisition we evaluated in two randomized, double-blind, active-controlled, multinational trus

partners, PURPOSE 2 enrolled participants in Argentina, Brazil, Mexico, Peni, Sv.
1. Agriculture of the United States, Participants who assisted negative for HVI-1.

Africa, Thalland, and the United States of the County of the

lymphocytes, and in in vivo rat micronucleus assays.

exposure to humans at the RHD of YEZTUGO.

surecuming and diasemne were rand. TRUVADA (N=1086) in a 2.1 ratio.

human exposure at the RHD, based on AUC. These tumors are considered to be a secondary response to chronic tissue initiation and granulomatous inflammation, due to the depot effect of lenacapavir following subcutaneous injection. The clinical relevance

Dosage & Administration

> Contraindications

Warnings & **Precautions** 

Adverse Reactions

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Use in Specific **Populations** 

**Clinical Studies** 

## 14. Clinical Studies

## 14 Clinical Studies: PURPOSE 1

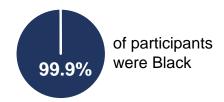
### **Study Design**

- PURPOSE 1 was in cisgender adolescent girls and young women aged 16–25 years in South Africa and Uganda who had unknown HIV-1 status at screening and were at risk of acquiring HIV-1a
- Participants who tested negative for HIV-1 were randomized to receive YEZTUGO (N=2134), once-daily DESCOVY (N=2136), or once-daily TRUVADA (N=1068) in a 2:2:1 ratio
- The use of DESCOVY (F/TAF) for the prevention of HIV in cisgender women is not approved. The safety and efficacy of this use have not been established

### **Baseline Characteristics**



Median participant age: 21 years (range: 16-26)



Baseline characteristics in the randomized participants were similar to those in the screened population

### **Outcomes/Results at Primary Analysis**

- HIV incidence per 100/PY was compared between participants receiving YEZTUGO and TRUVADA
- YEZTUGO demonstrated superiority over TRUVADA, with a 100% reduction in the risk of incident HIV-1 infection (Table 13; see next slide)
- YEZTUGO also demonstrated superiority in the risk of incident HIV-1 infection over bHIV









Approved for Use on 18 Aug 2025

SLD-LEN-NA-US-00012 MRC Approved 18-Aug-2025 External Use and Distribution Proactive Use

## 14. Clinical Studies

Indications & Usage

**PURPOSE 1** 

In PURPOSE 1, the median age of participants was 21 years (range, 16-26); and \$9.9%

were Black. Baseline characteristics in the randomized participants were similar to the

The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in

Overall HIV-1 Infection Outcomes in PURPOSE 13

participants randomized to YEZTUGO compared with the rate of incident HIV.1 infections per 100 person-years in participants randomized to TRUADA YEZTUGO. demonstrated superiority with a 100% reduction in the risk of incident HIV-1 infection

HIV-1 infections (incidence rate per 100 person- )

screened population. Over 99% of YEZTUGO injections were administered into the abdomen and each dose was administered in two locations. A total of 32 pregnant participants received YEZTUGO injections into the thigh and each dose was administered bilaterally (i.e., one injection in the right thigh and one injection in the left

Dosage & Administration

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Drug Interactions

Use in Specific **Populations** 

**Clinical Studies** 

## 14 Clinical Studies: PURPOSE 1 (continued)

### Table 13. Overall HIV-1 Incidence Outcomes in PURPOSE 1a

	YEZTUGO N=2134	TRUVADA N=1068	Rate Ratio (95% CI)
Person-years	1939	949	-
HIV-1 infections (incidence rate per 100 person-years)	0 (0.00)	16 (1.69)	YEZTUGO / TRUVADA: 0.000 (0.000, 0.101) <i>P</i> <0.0001



There were 2 incident infections among participants in the YEZTUGO arm of the PURPOSE 1 trial. Both occurred **after** the time of the primary analysis:

- 1 occurred in a participant after LEN exposures fell below the target concentration following discontinuation of YEZTUGO, and virus from this participant had no LEN resistance-associated capsid substitutions
- 1 occurred in a participant with viral loads that were too low for genotyping

<sup>a</sup>The determination of efficacy was based on planned interim analyses (which became the final analyses) following sequential testing of HIV-1 incidence for YEZTUGO compared to background followed by YEZTUGO compared to TRUVADA; all at alpha level of 0.0026 when 50% of randomized participants completed at least 52 weeks of follow-up or prematurely discontinued from the study; bInfections that occurred after starting YEZTUGO for HIX pproved for Use on 18 Aug 2025



## 14. Clinical Studies

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**Clinical Studies** 

A treatment-related increase in the incidence of malignant sarcoma at the injection site was observed in males and a treatment-related increase in combined benign fibroma and malignant fibrosarcoma at the injection site was observed in females, at the highest dose (927 mg/kg). This dose in rats resulted in an exposure approximately 44 times the human exposure at the RHD, based on AUC. These tumors are considered to be a secondary response to chronic tissue imitation and granulomatous inflammation, due to the depot effect of lenacapavir following subcutaneous injection. The clinical relevance of these findings are unknown.

Lenacapavir was not mutagenic in a battery of in vitro and in vivo genotoxicity assays, Leтасарачні was постіпнавдень, in a paniery of in vivro and in vivro genotonory assay, including microbial mutagenesis, chromosome aberration in human peripheral blood lymphocytes, and in in vivo rat micronucleus assays.

There were no effects on fertility, making performance or early embryonic developme. There were no enects on tertuiny, maning performance or early emoryonic generopmet, when lenacapavir was administered to rats at systemic exposures (AUC) 8 times the exposure to humans at the RHD of YEZTUGO.

The efficacy and safety of YEZTUGO in reducing the risk of HIV-1 acquisition. The efficacy and safety of YEZTUGU in reducing the risk of HIV-1 acquisition we evaluated in two randomized, double-blind, active-controlled, multinational trials

PURPUSE 1 was in osgender 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 years of age in South Africa and Uganda who had unknown the barriers years of age in South Africa and Uganda who have rom sexual arrival with make barriers years are new or a rock of armytima. HIV-1 based on sexual arrival with make barriers. years of age in South Africa and Uganda who had unknown HIV-1 status at screen and who were at risk of acquiring HIV-1 based on sexual activity with make partners and who were at risk of acquiring HIV-1 are creatives and have sline were randomized partners and have sline were randomized. and who were at risk of acquiring HiV.1 based on sexual activity with male partners of participants who tested negative for HIV.1 at screening and baseline were nactomized participants who tested negative for HIV.1 at screening and baseline were nactomized to participants who tested negative for HIV.1 at screening and baseline were nactorized to participants with the participant of the participants of t

TRUVADA (N=1086) in a 2:1 ratio.

## 14 Clinical Studies: PURPOSE 2



### **Study Design**

- PURPOSE 2 was in cisgender men, transgender women, transgender men and gender-nonbinary individuals aged ≥16 years with unknown HIV-1 status at screening and at risk of acquiring HIV-1a
- PURPOSE 2 enrolled participants in Argentina, Brazil, Mexico, Peru, South Africa, Thailand and the US
- Participants who tested negative for HIV-1 were randomized to receive YEZTUGO (N=2179) or oncedaily TRUVADA (N=1086) in a 2:1 ratio

### **Baseline Characteristics**



Median participant age: 29 years

(range: 17-74)

Non-White Hispanic/Latine Gender-diverseb



Baseline characteristics in the randomized participants were similar to those in the screened population

### **Outcomes/Results at Primary Analysis**

- HIV incidence per 100/PY was compared between participants receiving YEZTUGO and TRUVADA
- YEZTUGO demonstrated superiority over TRUVADA, with an 89% reduction in the risk of incident HIV-1 infection (Table 14; see next slide)
- YEZTUGO also demonstrated superiority in the risk of incident HIV-1 infection over bHIV

<sup>a</sup>Based on sexual activity with male partners; <sup>b</sup>Transgender women, transgender men and gender-nonbinary people bHIV, background HIV incidence; PY, person-years



## 14. Clinical Studies

Indications & Usage

Table 14.

Overall HIV-1 Infection Outcomes in PURPOSE 2<sup>a</sup>

The undernantiation or emissary was ussed on panned interm analyses (which became the fail analyses) following septiential testing of High-1 incidence for YETUGO compared to backgrand. Followed the VETTI YOU reconstructed to TO MAIN. and as debal local and in 1974 is when EDE value and the VETTI YOU reconstructed to TO MAIN. amanyses j roucowing sequential testing of http:// nooterce for YEZIUSU compared to background followed by YEZTUGO compared to TRIVADD, all at alpha level of 0.0026 when 5/% of randomized the compared of the control of the contro nationed by YE/LIUSO compared to TRUVADA, all at alpha level of 0.005 when 50% of randomic participants completed at least 52 weeks of follow-up or prematurely deconfined from the study YE/TUGO also demonstrated superiority in the risk of incident HIV-1 infection over tackground that is a followed by the study of th

YEZTUGO tablets 300 mg are beige, capsule-shaped, and film-coaled with "GSI" Each YEZTUGO bottle contains 4 tablets (NDC 61958-3401-1), a silica gel desccant, Each YELTUGU bottle contains 4 tablets (NDC 61958-3401-1), a slica gel desiccant, polyester coil, and is closed with a child resistant closure. Do not remove the desiccant resistant closure.

Store bottle at 20 °C - 25 °C (68 °F - 77 °F), excursions permitted lt. Store bottle at 20 °C –25 °C (68 °F – 77 °F), excursions permitted to 15 °C –30 °C (59 °F – 96 °F) (see USP Controlled Room Temperature).

YETTUGO injection is packaged in a dosing kit (NDC 61958-3402-1) containing with a surface of the packaged in a dosing kit (NDC 61958-3402-1) containing sufficient volume to allow within is serile.

2 single dose clear glass vials, each containing sufficient volume to solution is serile.

of 463.5 mg/l 5 mL (303 mg/mL) of teracagoavir. The injection solution is serile with a containing sufficient particles. Vials are sealed with a containing series with a containing series of the containing series with a containing series of the containing series with a containing series of the containing n is packaged in a dosing kit (NDC 61958-3402-1) contains

Suppler and auminium oversear with the or cap.

2 disposable syringes, 2 withdrawal needles (18-gauge, 1½ inch).

3 disposable syringes, 2 withdrawal needles (19-gauge, 1½ inch).

3 disposable syringes, 2 withdrawal needles (19-gauge, 1½ inch).

16 HOW SUPPLIED/STORAGE AND HANDLING

YEZTUGO TRUVADA Rate Ratio (95% CI)

(0.93)

TRUVADA: 0.111 (0.024, 0.513)

p = 0.00245

Dosage & Administration

> Contraindications

Warnings & Precautions

> Adverse Reactions

Drug Interactions

Use in Specific Populations |

**Clinical Studies** 

14	<b>Clinical Studies:</b>	PURPOSE 2	(continued)



### Table 14. Overall HIV-1 Incidence Outcomes in PURPOSE 2<sup>a</sup>

	YEZTUGO N=2179	TRUVADA N=1086	Rate Ratio (95% CI)
Person-years	1938	967	-
HIV-1 infections (incidence rate per 100 person-years)	2 (0.1)	9 (0.93)	YEZTUGO / TRUVADA: 0.111 (0.024, 0.513) <i>P</i> =0.00245



There were 3 incident infections among participants in the YEZTUGO arm of the PURPOSE 2 trial:

- 1 occurred **after** the time of primary analysis
- LEN resistance-associated substitutions were detected in viruses from all 3 participants: 2 with N74D, and 1 with Q67H/K70R

<sup>a</sup>The determination of efficacy was based on planned interim analyses (which became the final analyses) following sequential testing of HIV-1 incidence for YEZTUGO compared to background followed by YEZTUGO compared to TRUVADA; all at alpha level of 0.0026 when 50% of randomized participants completed at least 52 weeks of follow-up or prematurely discontinued from the study; bInfections that occurred after starting YEZTUGO for HIX pproved for Use on 18 Aug 2025



## **Appendix**

## 2. Dosage and Administration

Indications & Usage

Dosage & Administration

Contraindications

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Drug Interactions

Use in Specific Populations

Clinical Studies

	Therapy with Strong CYP3	mental Doses of YEZTUGO	
Maintain Scheduled		Dosage .	
Continuation Injection Dosing	Time	Supplemental dosage: Step 1	
Continue to administer once every 6-months	On day strong CYP3A, inducer is initiated (which should be at least 2 days after YEZTUGO is first initiated)	927 mg subcutaneously (2 x 15 mg) injections) and 600 mg orally (2 x 300 mg tablets)	
scheduled continuation dosing	On day after strong CYP3A inducer is initiated	600 mg orally (2 x 300 mg	
subcutaneously (2 1.5 mL injections) (see Table 1), plus administer	If strong CYP3A inducer is co-administered for longer than 6 months	Every 6-months recurred to administer CYP3A inducer, continue to administer supplemental doses of YEZTUGO as described above in Steps 1 and 2. described above in Steps 1 and 2.	
	dations are not available for the intu- dations are not available for the intu- yP3A inducers, nor in individuals re- eks.	ceiving the weekly value of the weekly value o	
D. 20	Decommendations Moderate	CYPSA III	
Dos Dos	ing Therapy with its	polemental Doses on posage	
I apri	Schedule		
Maintain Schedule	d Time	Supplementaneously (1 x 1.2	
Maintain 300 Continuation Injection Dosing		Supplemental dosage 453.5 mg subcutaneously (1 x 1.5 mL injection)  Subsequent supplemental dosage Subsequent supplemental dosage Subsequent supplemental dosage	
Continue to	100	Every 6-moducer, continued YEZTUGO	
Joinister Olive	AVD3A INDUCE	City shortenia and above	
Continue to administer once every 6-months scheduled continuation dosin of YEZTUCO 927 of YEZTUCO 927 subcutaneously (subcutaneously (subcutan	g mg If moderate CYP3A inducer is co-administered for longer co-administered for longer than 6 months	Supplemental vision of supplemental vision of supplemental vision of supplemental vision of supplemental vision relation of vicinity of supplemental vision relation of vicinity of supplemental vision relations of vicinity of vision vi	

2.5 Dosage Modifications for Co-administration with Strong or Moderate CYP3A Inducers

## Table 4. Dosing Recommendations for Individuals Receiving YEZTUGO and Initiating Therapy with Strong CYP3A Inducers<sup>a</sup>

	Maintain Scheduled Continuation Injection Dosing	Schedule for <u>Supplemental</u> Doses of YEZTUGO		
	Continue to administer once Q6M scheduled continuation dosing of YEZTUGO (see <b>Table 1</b> ), plus administer supplemental doses of	Time	Dosage	
		On day strong CYP3A inducer is initiated (≥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)	
	YEZTUGO as shown here:	On day after strong CYP3A inducer is initiated	Supplemental dosage: Step 2 600 mg orally (2 × 300 mg tablets)	
		If strong CYP3A inducer is co-administered for >6 months	Subsequent supplemental dosage Q6Mb from initiation of 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 Q6M scheduled continuation injection dosing of YEZTUGO (see <b>Table 1</b> )		

<sup>a</sup>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 **Table 2**); <sup>b</sup>26 weeks ±2 weeks CYP3A, cytochrome (P450) 3A; Q6M, every 6 months

BACK (n) NEXT

Approved for Use on 18 Aug 2025

## 2. Dosage and Administration

Indications & Usage

Dosing Recommendations for Individuals Receiving YEZTUGO and

Schedule for Supplemental Doses of YEZTUGO

Dosing Recommendations for Individuals Receiving YEZTUGO and

Initiating Therapy with Moderate CYPAA Inducess

Supplemental dosage: Step 1

927 mg subcutaneously (2 x 1.5 mL

Supplemental dosage: Step 2

Initiating Therapy with Strong CYP3A Inducers

On day strong CYP3A inducer is initiated (which

should be at least 2 days

Maintain Scheduled

Injection Dosing

Continue to administer once

every 6-months scheduled continuation dosing

of YEZTUGO 927 m subcutaneously (2)

1.5 mL injections) (see Table 1), plus

Dosage & Administration

> Contraindications

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Use in Specific Populations

Clinical Studies

## 2.5 Dosage Modifications for Co-administration with Strong or Moderate **CYP3A Inducers**

## Table 5. Dosing Recommendations for Individuals Receiving YEZTUGO and Initiating Therapy with Moderate CYP3A Inducers<sup>a</sup>

Maintain Scheduled Continuation Injection Dosing	Schedule for <u>Supplemental</u> Doses of YEZTUGO	
Continue to administer once	Time	Dosage
Q6M scheduled continuation dosing of YEZTUGO (see <b>Table 1</b> ), plus administer supplemental doses of YEZTUGO as shown here:	On day moderate CYP3A inducer is initiated	Supplemental dosage 463.5 mg subcutaneously (1 x 1.5 mL injection)
	If moderate CYP3A inducer is co-administered for >6 months	Subsequent supplemental dosage Q6Mb from initiation of moderate CYP3A inducer, continue to administer a supplemental dose of YEZTUGO as described above
		ate CYP3A inducer, continue the Q6M scheduled ction dosing of YEZTUGO (see <b>Table 1</b> )

<sup>a</sup>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 Table 2); b26 weeks ±2 weeks CYP3A, cytochrome (P450) 3A; Q6M, every 6 months







Approved for Use on 18 Aug 2025

# YEZTUGO® (lenacapavir) for HIV-1 PrEP

**Navigating the US Prescribing Information**