Gilead Sciences, Inc. is providing this document to you, a US Healthcare Professional, in response to your unsolicited request for medical information.

GILEAD | Medical Information

Yeztugo® (lenacapavir) Use in Pregnancy and Lactation

This document is in response to your request for information regarding the use of Yeztugo® (lenacapavir [LEN]) during pregnancy and lactation.

This document includes content from, or references to, clinical practice guidelines, and inclusion should not be interpreted as a treatment recommendation or an endorsement of the guidelines by Gilead Sciences, Inc.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The use of FTC/TAF for prevention of HIV-1 in individuals at risk of HIV-1 from receptive vaginal sex is investigational and has not been approved by any regulatory authority. The full indication, important safety information, and boxed warning(s) are available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Summary

Product Labeling[1]

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to LEN during pregnancy. Healthcare providers are encouraged to register individuals by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.

Available data from a randomized, controlled trial (PURPOSE 1) with LEN use during pregnancy 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 LEN-exposed pregnancies did not exceed the background prevalence rates.

LEN is present in human milk. LEN was detected at very low levels in infants who were breastfed by individuals who became pregnant while receiving LEN. No adverse effects of LEN in breastfed infants have been observed. It is not known if LEN affects milk production.

Clinical Data on LEN Use During Pregnancy

PURPOSE 1 is an ongoing, phase 3, double-blind, randomized, active-controlled study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TAF or FTC/TDF (control) for HIV-1 PrEP in cisgender women and adolescent girls in South Africa and Uganda.[2]

- At the data cutoff of May 8, 2024, there were 509 pregnancies among 487 participants: 193 pregnancies in the LEN group, 218 in the FTC/TAF group, and 98 in the FTC/TDF group. By the end of the RBP, the total had increased to 712 pregnancies among 665

participants: 269 pregnancies in the LEN group, 302 in the FTC/TAF group, and 141 in the FTC/TDF group.[3,4]

- The study authors determined that frequency of pregnancy outcomes – including rates of spontaneous abortions, stillbirths, preterm births, and small-for-gestational-age births – as well as congenital anomalies observed in the LEN group were consistent with background rates.[3,5-7]
- HIV acquisition occurred in 4 pregnant participants in the FTC/TAF group and 1 pregnant participant in the FTC/TDF group. There were no HIV cases among pregnant participants randomized to the LEN group. No cases of vertical transmission were observed.[3]
- In a nested PK substudy of participants who were randomly assigned to the LEN group and became pregnant during the study, LEN concentrations remained generally consistent throughout pregnancy and postpartum, with no evident trimester-related changes. Subsequent population PK analyses demonstrated no statistically significant differences in LEN exposure when comparing pregnancy trimesters, postpartum status, and non-pregnant individuals.[3]

Pregnancy outcomes from the PURPOSE 2 study have not been published.[8]

Clinical Data on LEN Use During Lactation[3]

Further PK analyses showed LEN exposures were similar between pregnant and non-pregnant participants. LEN was found in breast milk, but LEN concentrations were very low in breastfed infants.

Product Labeling[1]

Use in Specific Populations

Pregnancy

Pregnancy exposure registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to LEN during pregnancy. Healthcare providers are encouraged to register individuals by calling the APR at 1-800-258-4263.

Risk summary

Available data from a randomized, controlled trial (PURPOSE 1) with LEN use during pregnancy 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 LEN-exposed pregnancies did not exceed the background prevalence rates. The risk estimates are imprecise due to small numbers of exposed pregnancies. There is an increased risk of HIV-1 transmission from the mother to the child during acute HIV-1 infection. In animal reproduction studies, no adverse developmental effects were observed when LEN was administered to rats and rabbits at exposures (AUC) ≥7 times the exposure in humans at the recommended human dose of LEN.

The APR has been established to monitor for birth defects following prenatal exposure to ARVs. The APR uses the MACDP as the US reference population for birth defects in the general population. The background rate for major birth defects is 2.7% in the MACDP. The

rate of miscarriage for individual drugs is not reported in the APR. In the US general population, the estimated background risk of miscarriage in clinically recognized pregnancies is 15% to 20%. The MACDP evaluates mothers and infants from a limited geographic area and does not include outcomes for births that occurred at <20 weeks gestation.

Clinical considerations: disease-associated maternal and/or embryo/fetal risk

Published studies indicate an increased risk of HIV-1 infection during pregnancy and an increased risk of mother-to-child transmission during acute HIV-1 infection. In women at risk of acquiring HIV-1, consideration should be given to methods to prevent acquisition of HIV-1, including continuing or initiating LEN for HIV-1 PrEP, during pregnancy.

Data: human data

In a randomized, controlled trial in Uganda and South Africa (PURPOSE 1), there were 208 pregnancies exposed to LEN with known outcomes and 132 deliveries (both live and non-live). In the active control arm of PURPOSE 1, there were 109 pregnancies exposed to FTC/TDF with known outcomes and 61 deliveries (both live and non-live). The adverse pregnancy outcomes of spontaneous abortion, stillbirth, preterm birth, and small for gestational age were similar across both treatment groups.

There were two major birth defects in the LEN arm. Both were ventricular septal defects. This resulted in a rate of major birth defects that fell within the background prevalence rate for major birth defects.

Concentrations of LEN during each trimester of pregnancy and postpartum were comparable to those in non-pregnant participants.

Lactation

Risk summary

LEN is present in human milk. LEN was detected at very low levels in infants who were breastfed by individuals who became pregnant while receiving LEN. No adverse effects of LEN in breastfed infants have been observed. It is not known if LEN affects milk production.

In women without HIV-1 infection, the developmental and health benefits of breastfeeding and the mother's clinical need for LEN for HIV-1 PrEP should be considered along with any potential adverse effects on the breastfed child from LEN and the risk of HIV-1 acquisition due to nonadherence and subsequent mother-to-child transmission.

Data: human data

The median LEN concentration in human breast milk to maternal plasma ratio in participants (n=8) who received LEN was 0.63 (range: 0.29–1.9). The median infant-to-mother plasma ratio for LEN in infants (n=10) who were breastfed by individuals receiving LEN from 0 to <13 weeks after delivery was 0.06 (range: 0.01–0.2).

Clinical Data on LEN Use During Pregnancy

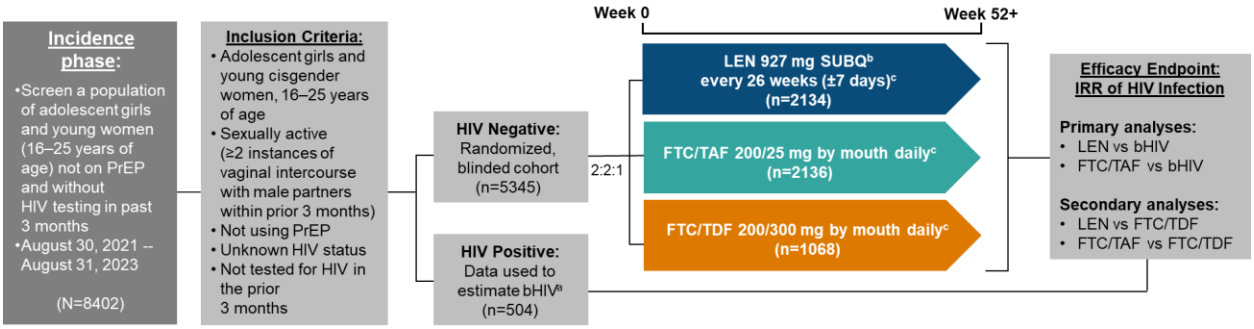
PURPOSE 1

Study design

PURPOSE 1 (NCT04994509) is an ongoing, phase 3, double-blind, randomized, active-controlled study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TAF for HIV-1 PrEP in cisgender women and adolescent girls across South Africa and Uganda. Additionally, a third group was assigned once-daily oral FTC/TDF, which served as the active control (Figure 1). Participants who discontinued blinded study drug were given the option to take open-label FTC/TDF. Randomized participants had body weight ≥35 kg and eGFR ≥60 mL/min.[2]

Testing for HIV in the randomized cohort was conducted at Weeks 4, 8, and 13 and every 13 weeks thereafter.[2] Urine pregnancy testing was performed at every study visit. In the event of a positive urine pregnancy test, serum pregnancy testing was conducted for confirmation. Individuals were excluded if they were pregnant or lactating prior to administration of first dose of study drug.[9] Contraception was not required but was provided for participants. Participants could continue to receive the study drug if they became pregnant after a reconsent process on potential risks and benefits, and pregnant participants were permitted to receive SUBQ LEN injection in the thigh.[2,9] If a participant gave birth while in the study, infant health follow-up was conducted for 1 year after birth or until the mother's participation in the study ended. Participants were allowed to breastfeed in the study.[9]

Figure 1. PURPOSE 1: Study Design[2]



Abbreviations: bHIV=background HIV; IRR=incidence rate ratio.
[a]The bHIV was determined based on a cross-sectional incidence estimate derived from rates of recent HIV in 8094 screened participants; these participants were not followed longitudinally.
[b]All participants randomly assigned to receive LEN received an initial loading dose of LEN, which consisted of 600 mg (two 300-mg tablets) administered on Days 1 and 2.
[c]Participants in the LEN SUBQ group also received placebo FTC/TAF or placebo FTC/TDF (2:1), and participants in the FTC/TAF and FTC/TDF groups also received placebo LEN oral loading doses and placebo SUBQ LEN.

A total of 5345 participants were randomly assigned and received ≥1 dose of study drug. Baseline (at randomization) characteristics among the three groups were similar (Table 1). Overall retention in the study was high and similar across groups, with 4855/5020 participants (96.7%) completing 26 weeks of follow-up, 2439/2612 participants (93.4%) completing 52 weeks, and 39/43 participants (91%) completing 104 weeks.[2]

An independent committee determined that the planned interim efficacy analysis (when 50% of participants had completed ≥52 weeks of follow-up; data cutoff for clinical data, May 28, 2024, and data cutoff for laboratory data, May 29, 2024) met the prespecified criteria for stopping the randomized, blinded portion of the trial. Starting July 8, 2024, all participants were offered open-label LEN.[2]

Table 1. PURPOSE 1: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		LEN (n=2138)	FTC/TAF (n=2137)	FTC/TDF (n=1070)
Age	Median (range), years	21 (16–25)	21 (16–26)	21 (16–25)
	16 or 17 years of age, n (%)	56 (2.6)	45 (2.1)	23 (2.1)
Black race, n (%)		2135 (99.9)	2136 (>99.9)	1068 (99.8)
Living with primary partner, n/N (%)		148/2136 (6.9)	132/2134 (6.2)	73/1069 (6.8)
Previous use of PrEP, n (%)		143 (6.7)	121 (5.7)	71 (6.6)
Previously tested for HIV, n (%)		1713 (80.1)	1731 (81)	860 (80.4)
Time since last HIV test, median (IQR), months		6.8 (4.7–11.5)	6.6 (4.8–11)	6.5 (4.6–11)
Sexually transmitted infections, n (%)	*Chlamydia trachomatis*	520 (24.3)	562 (26.3)	263 (24.6)
	Neisseria gonorrhoeae	197 (9.2)	178 (8.3)	90 (8.4)
	Trichomonas vaginalis	154 (7.2)	165 (7.7)	82 (7.7)
	Syphilis	57 (2.7)	63 (2.9)	29 (2.7)
Country, n (%)	South Africa	1809 (84.6)	1790 (83.8)	909 (85)
	Uganda	329 (15.4)	347 (16.2)	161 (15)

Pregnancy outcomes

In a planned substudy of all pregnancies confirmed by the primary analysis data cutoff (May 8, 2024), pregnancy outcomes were followed through March 26, 2025. Evaluated endpoints included pregnancy outcomes, HIV acquisitions, AEs during pregnancy and postpartum, and observed and model-derived LEN plasma concentrations by pregnancy trimester and postpartum period; pregnancy outcomes and infant congenital anomalies were assessed by participant report and medical record review.[3] In addition, supplemental analyses included all pregnancies diagnosed through the end of the RBP.[4] Pregnancy outcomes for these pregnancies were followed through October 6, 2025, including participants who entered the lenacapavir open-label extension.[3]

At the data cutoff of May 8, 2024, there were 509 pregnancies among 487 participants: 193 pregnancies in the LEN group, 218 in the FTC/TAF group, and 98 in the FTC/TDF group (Table 2).[3] The study authors determined that pregnancy outcomes – including rates of spontaneous abortions, stillbirths, preterm births, and small-for-gestational-age births – were within the expected background rates reported in South Africa and Uganda.[3,5,6]

Overall, 10 congenital abnormalities were reported: LEN, n=6 (congenital hemangioma, umbilical hernia, left hand polydactyly, perimembranous ventricular septal defect, congenital ventricular septal defect, and congenital reducible umbilical hernia; each, n=1); FTC/TAF, n=4 (infant bilateral hydrocele; right inguinal hernia, umbilical hernia, and neonatal jaundice; Down syndrome; and clubfoot; each, n=1).[10] All congenital anomalies were assessed by investigators as unrelated to study drug except for one ventricular septal defect in the LEN group, which was considered treatment-related.[3] The participant with an infant with polydactyly had a reported strong maternal family history of polydactyly.[4] The heterogeneous anomalies observed were considered consistent with background incidence and did not suggest a drug-related pattern.[3,7]

Table 2. PURPOSE 1: Pregnancy Outcomes[3]

Pregnancy Outcomes, n or n/N (%)	LEN (n=184)	FTC/TAF (n=208)	FTC/TDF (n=95)	Total (n=487)
Participants with confirmed pregnancies	184	208	95	487
Confirmed pregnancies	193	218	98	509

Pregnancy Outcomes, n or n/N (%)	LEN (n=184)	FTC/TAF (n=208)	FTC/TDF (n=95)	Total (n=487)
Pregnancy incidence rate per 100 person-years[a]	10.0	11.2	10.2	10.5
Total pregnancy outcomes[b]	195	219	98	512
Live births	128/195 (66)	119/219 (54)	56/98 (57)	303/512 (59)
At term (≥37 to ≤42 weeks' gestation)	105/128 (82)	93/119 (78)	40/56 (71)	238/303 (79)
Preterm (<37 weeks' gestation)	14/128 (11)	19/119 (16)	11/56 (20)	44/303 (15)
Post-term (>42 weeks' gestation)	9/128 (7)	7/119 (6)	5/56 (9)	21/303 (7)
Congenital abnormality[c]	6/127 (5)	4/117 (3)	0	10/300 (3)
Small for gestational age[d]	11/128 (9)	12/119 (10)	9/56 (16)	32/303 (11)
Pregnancy losses	60/195 (31)	89/219 (41)	41/98 (42)	190/512 (37)
Stillbirth[e]	5/195 (3)	6/219 (3)	3/98 (3)	14/512 (3)
Induced or elective abortions	35/195 (18)	50/219 (23)	23/98 (23)	108/512 (21)
Spontaneous abortions[f]	20/195 (10)	33/219 (15)	15/98 (15)	68/512 (13)
Pregnancies with unknown outcomes[g]	7/195 (4)	11/219 (5)	1/98 (1)	19/512 (4)

[a]Pregnancy incidence rate is the number of confirmed pregnancies divided by person-years of follow-up; person-years of follow-up are the sum of all participants' total number of years (365.25 days) in the randomised, masked phase for the primary analysis (LEN 1934.1 years, FTC/TAF 1943.5 years, FTC/TDF 956.7, and total 4834.4).
[b]Total pregnancy outcomes includes the number of livebirths, pregnancy losses, and pregnancies with unknown outcome; one pregnancy can include multiple outcomes or births (three sets of twins: two sets in participants randomly allocated to LEN [one set of stillborn twins and one set of liveborn healthy twins] and one set in participants randomly allocated to FTC/TAF [liveborn and premature]); birth outcomes are reported for each individual infant.
[c]Includes one infant reported to have had a healthy outcome at birth whose congenital abnormality of umbilical hernia was first detected at approximately 4 months of age.
[d]Small for gestational age was defined as a weight under the 10th percentile by sex and gestational age.
[e]Stillbirth or intrauterine fetal demise defined as occurring at 20 weeks' gestation or longer. There was one set of stillbirth twins in the LEN group.
[f]Spontaneous abortion defined as occurring at less than 20 weeks' gestation; estimated gestational age data are missing for one infant in the FTC/TAF group.
[g]Unknown due to participant discontinuation for the following reasons: pregnancy (LEN [two]; FTC/TAF [two]); investigator's discretion (FTC/TAF [one]); withdrawal of consent (LEN [five] and FTC/TAF [four]); and loss to follow-up (FTC/TAF [four]; FTC/TDF [one]).

Among pregnant participants, HIV acquisition occurred in 4 participants in the FTC/TAF group and 1 participant in the FTC/TDF group. There were no HIV cases among pregnant women randomly assigned to the LEN group. No cases of vertical transmission were observed.[3]

Overall, 44/132 participants (33.3%) who received ≥1 dose of SUBQ LEN during pregnancy or postpartum reported an ISR.[3] All reported ISRs were Grade 1 or 2 in severity, and the most frequently reported ISRs were nodules (n=35; 26.5%) and injection site pain (n=17; 12.9%).[3,10] Additional safety outcomes during pregnancy and postpartum are presented in Table 3.[3]

Table 3. PURPOSE 1: Safety Outcomes During Pregnancy and Postpartum[3]

AEs During Pregnancy and Postpartum,[a] n (%)	LEN (n=184)	FTC/TAF (n=208)	FTC/TDF (n=95)
Any AEs[b]	135 (73)	142 (68)	68 (72)
Grade ≥2	112 (61)	112 (54)	55 (58)
Grade ≥3	36 (20)	39 (19)	22 (23)

AEs During Pregnancy and Postpartum,[a] n (%)		LEN (n=184)	FTC/TAF (n=208)	FTC/TDF (n=95)
SAEs[b]		41 (22)	50 (24)	22 (23)
AEs leading to discontinuation of study drug[b]		1 (1)[c]	0	0
AEs occurring in ≥5% of participants in any randomized group[d]	Urinary tract infection	39 (21)	34 (16)	27 (28)
	Upper respiratory tract infection	20 (11)	16 (8)	6 (6)
	Vulvovaginal candidiasis	17 (9)	22 (11)	8 (8)
	Genitourinary chlamydia infection	16 (9)	10 (5)	8 (8)
	Vaginal discharge	13 (7)	6 (3)	6 (6)
	Vomiting	10 (5)	16 (8)	9 (9)
	Headache	10 (5)	15 (7)	4 (4)
	Malaria	10 (5)	6 (3)	4 (4)
	Nausea	7 (4)	10 (5)	8 (8)
	Morning sickness	3 (2)	5 (2)	6 (6)
	Death	0	0	0

[a]Adverse events and laboratory abnormalities that are reported here were those that occurred in participants who had received at least one dose of a study drug or placebo. Adverse events were coded according to the Medical Dictionary for Regulatory Activities (version 27.1) and graded according to the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events version 2.1. The pregnancy and postpartum period were defined as the time from the last menstrual period through to 6 weeks after the pregnancy outcome.
[b]Injection site reactions to non-study medications are included, but injection site reactions to the study SUBQ injection are excluded.
[c]Spontaneous abortion (investigator assessed as unrelated to study drug).
[d]Injection site reactions and spontaneous abortions have been excluded.

In addition, supplemental pregnancy and birth outcome data for all pregnancies diagnosed through the end of the RBP were reported. A total of 712 pregnancies were identified among 665 participants, including 269 pregnancies in the LEN group, 302 in the FTC/TAF group, and 141 in the FTC/TDF group (Table 4).[3,4] Pregnancy and birth outcomes in this expanded follow-up period were generally consistent with those observed in the primary analysis.[3]

Table 4. PURPOSE 1: Supplemental Pregnancy Outcomes Through the End of the RBP[4]

Pregnancy Outcomes, n or n (%)	LEN (n=253)	FTC/TAF (n=280)	FTC/TDF (n=132)	Total (n=665)
Participants with confirmed pregnancies	253	280	132	665
Confirmed pregnancies	269	302	141	712
Total Pregnancy Outcomes[a]	272	304	141	717
Live births	172 (63)	167 (55)	84 (60)	423 (59)
At term (≥37 to ≤42 weeks' gestation)	139 (81)	127 (76)	61 (73)	327 (77)
Preterm (<37 weeks' gestation)	22 (13)	28 (17)	18 (21)	68 (16)
Post-term (>42 weeks' gestation)	11 (6)	12 (7)	5 (6)	28 (7)
Congenital abnormality	6 (3)	7 (4)	1 (1)	14 (3)
Small for gestational age[b]	22 (13)	15 (9)	10 (12)	47 (11)
Pregnancy losses	91 (33)	123 (40)	53 (38)	267 (37)
Stillbirth[c]	9 (3)	8 (3)	4 (3)	21 (3)
Induced or elective abortions	49 (18)	71 (23)	28 (20)	148 (21)
Spontaneous abortions[d]	33 (12)	44 (14)	21 (15)	98 (14)

Pregnancy Outcomes, n or n (%)	LEN (n=253)	FTC/TAF (n=280)	FTC/TDF (n=132)	Total (n=665)
Pregnancies with Unknown Outcomes[e]	9 (3)	14 (5)	4 (3)	27 (4)

[a]A single pregnancy may include multiple outcomes/births (five sets of twins: three sets in participants randomized to LEN and two sets in participants randomized to FTC/TAF). Birth outcomes were reported for each individual infant.
[b]Small for gestational age was defined as weight <10th percentile by sex/gestational age.
[c]Stillbirth/intrauterine fetal demise defined as occurring ≥20 weeks' gestation. There was one set of stillbirth twins in the LEN group.
[d]Spontaneous abortion defined as occurring at <20 weeks' gestation.
[e]Unknown due to participant discontinuation for the following reasons: pregnancy (LEN, n=3; FTC/TAF, n=4; FTC/TDF, n=1); investigator's discretion (FTC/TAF, n=2); withdrew consent (LEN, n=5; FTC/TAF, n=5); lost to follow-up (FTC/TAF, n=2; FTC/TDF, n=1); completed study (LEN, n=1; FTC/TAF, n=1; FTC/TDF, n=1); ongoing pregnancy (FTC/TDF, n=1).

Population PK Analysis of LEN in Pregnancy

A nested PK substudy of participants who were randomly assigned to the LEN group and became pregnant during the study was conducted to assess systemic LEN concentrations during pregnancy and postpartum, as well as LEN concentrations in breast milk and infants. Maternal plasma PK samples were collected in regular intervals throughout the first, second, and third trimesters, and maternal plasma, infant plasma, and breast milk samples were obtained at approximately 3 and 6 months postpartum.[3]

Overall, 601 participants were included in the population PK analysis, including 296 participants who became pregnant while receiving LEN and had at least one quantifiable PK sample collected during pregnancy. Pregnant participants received SUBQ LEN injections in the thigh or abdomen.[3] At Weeks 26, 52, and 78, C_{trough} data were available from 107 first-trimester, 99 second-trimester, 59 third-trimester, and 65 postpartum visits.[10]

No observable trimester-related trends in LEN were identified across pregnancy trimesters or during the postpartum period (Figure 2). Model-derived LEN C_{max} and C_{trough} concentrations were comparable across participants between pregnancy trimesters, postpartum, and non-pregnant individuals (Figure 3). Population PK analyses further demonstrated that gestational age, pregnancy trimester, and postpartum status were not statistically significant covariates of LEN exposure. LEN PK were also similar when LEN was injected in the thigh or the abdomen.[3]

Figure 2. PURPOSE 1: Observed LEN Concentrations (up to week 104, stratified by pregnancy groups, for participants who took lenacapavir on time)[3]

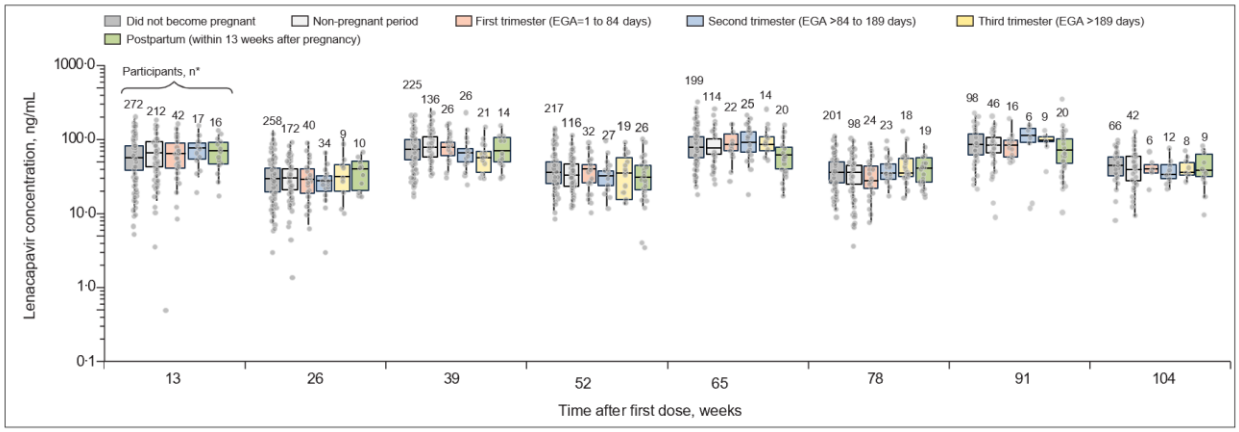
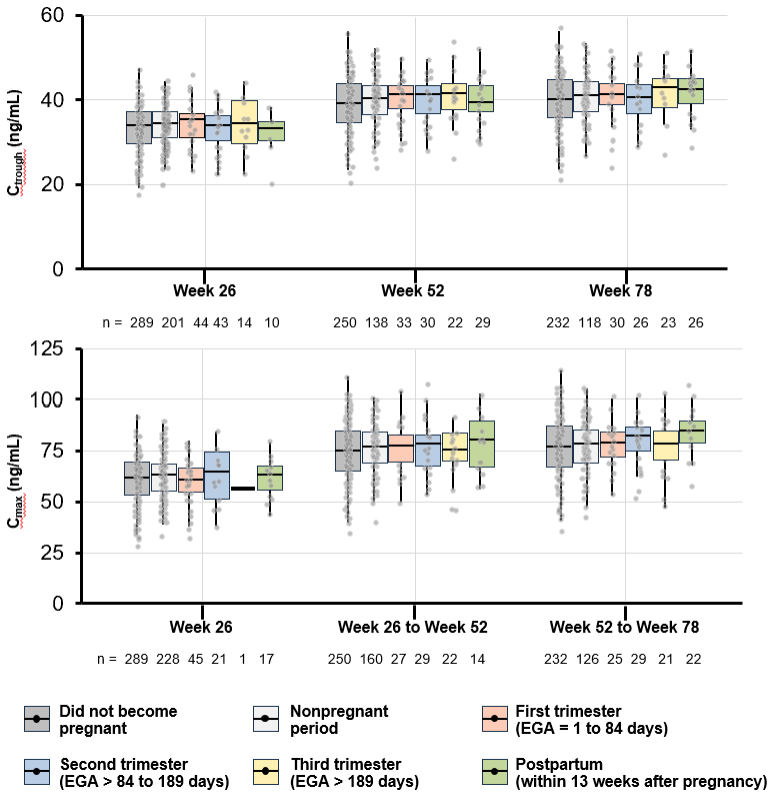


Figure 3. PURPOSE 1: Model-derived LEN C_{max} and C_{trough} Concentrations[4]



PURPOSE 2

Study design

PURPOSE 2 (NCT04925752) is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN or once-daily oral FTC/TDF for HIV-1 PrEP in cisgender gay, bisexual, and other men; TGW; TGM; and GNB individuals in Argentina, Brazil, Mexico, Peru, South Africa, Thailand, and the US who have condomless receptive anal sex with partners assigned male at birth (N=3265).[8]

Participants of childbearing potential were required to have a negative pregnancy test at the screening visit and on Day 1 prior to receiving the study intervention. They must not have been breastfeeding at study entry. Participants were also required to use an acceptable form of contraception during trial participation.[11]

Pregnancy outcomes from PURPOSE 2 have not been published.[8]

APR Data on LEN Use in Pregnancy[12]

Healthcare providers are encouraged to register individuals by calling the APR at 1-800-258-4263.

The APR is intended to provide an early signal of teratogenicity associated with prenatal use of ARV therapy for those drugs monitored in the registry. The APR contains analyses of voluntary, prospective reports of prenatal exposures to ARVs. The women included in this analysis were primarily HIV-1 monoinfected.

APR Advisory Committee Consensus for all ARVs

In reviewing all reported defects from the prospective registry, informed by clinical studies and retrospective reports of ARV exposure, the registry has found no apparent increases in the frequency of specific defects with first-trimester exposures and no pattern to suggest a common cause. While the registry population exposed and monitored to date is not sufficient to detect an increase in the risk of relatively rare defects, these findings should provide some assurance when counseling patients. However, potential limitations of registries such as this should be recognized. The registry is ongoing. Given the use of new therapies about which data are still insufficient, health care providers are strongly encouraged to report eligible patients to the registry at SM_APR@APRegistry.com via the data forms available at www.APRegistry.com.

LEN data in the APR

The June 2026 interim report includes prospective reports of 24,898 pregnancies with follow-up data through January 31, 2026. The current APR reported 3 cases of LEN exposure during the first trimester and 4 cases during the second or third trimester. No birth defects were reported among these exposed cases. Currently, there are insufficient exposure data on LEN to detect a pattern of increase in risk of birth defects.

Clinical Data on LEN Use During Lactation

PURPOSE 1: PK Substudy[3]

LEN was found in breast milk, but LEN concentrations were very low in breastfed infants. In 102 matched pairs, the median (IQR) breastmilk-to-maternal plasma ratio was 0.52 (0.38–0.77). In 98 matched pairs, the median (IQR) breastfed-infant-to-maternal plasma ratio was 0.02 (0.01–0.05). No adverse effects were identified among breastfed infants exposed to LEN.

Clinical Guidelines on PrEP Use in Pregnancy

Please see the US Department of Health and Human Services (DHHS) guidelines for recommendations regarding the use of PrEP to prevent HIV during periconception, antepartum, and postpartum periods: https://clinicalinfo.hiv.gov/en/guidelines/perinatal/pre-exposure-prophylaxis-prep-prevent-hiv. Please note, the guidelines are not specific to LEN.

References

1. YEZTUGO®, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA. Revised: June. 2025.
2. Bekker LG, Das M, Abdool Karim Q, et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. *N Engl J Med.* 2024;391(13):1179-1192.
3. Bekker LG, Moodley D, Diallo DD, et al. HIV acquisitions, safety, and pharmacokinetics of lenacapavir for HIV pre-exposure prophylaxis in pregnant and lactating women (PURPOSE 1): a substudy of a phase 3, randomised controlled trial. *Lancet HIV.* 2026.
4. Bekker LG, Moodley D, Diallo DD, et al. HIV acquisitions, safety, and pharmacokinetics of lenacapavir for HIV pre-exposure prophylaxis in pregnant and lactating women (PURPOSE 1): a substudy of a phase 3, randomised controlled trial. [Supplementary Appendix]. 2026:1-14.
5. Balkus JE, Neradilek M, Fairlie L, et al. Assessing pregnancy and neonatal outcomes in Malawi, South Africa, Uganda, and Zimbabwe: Results from a systematic chart review. *PLoS One.* 2021;16(3):e0248423.
6. Lokken EM, Mathur A, Bunge KE, et al. Pooled Prevalence of Adverse Pregnancy and Neonatal Outcomes in Malawi, South Africa, Uganda, and Zimbabwe: Results From a Systematic Review and Meta-Analyses to Inform Trials of Novel HIV Prevention Interventions During Pregnancy. *Front Reprod Health.* 2021;3:1-13.
7. Toobaie A, Yousef Y, Balvardi S, et al. Incidence and prevalence of congenital anomalies in low- and middle-income countries: A systematic review. *J Pediatr Surg.* 2019;54(5):1089-1093.
8. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons. *N Engl J Med.* 2025;392(13):1261-1276.
9. Bekker LG, Das M, Abdool Karim Q, et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women [Protocol]. *N Engl J Med.* 2024:1-672.

10. Bekker L-G, Moodley D, Harkoo I, et al. Inclusion of Pregnant and Lactating People in the PURPOSE 1 Study: Efficacy, Safety, and Pharmacokinetics. [Presentation]. Paper presented at: 13th International AIDS Society (IAS) Conference on HIV Science; July 13–17, 2025; Kigali, Rwanda.
11. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons [Protocol]. *N Engl J Med.* 2024.
12. Antiretroviral Pregnancy Registry Steering Committee. *The Antiretroviral Pregnancy Registry Interim Report: 01 January 1989 Through 31 January 2026. Morrisville, NC.* 2026.

Abbreviations

AE=adverse event
APR=Antiretroviral Pregnancy Registry
ARV=antiretroviral
AUC=area under the time-concentration curve
C_{trough}=trough concentration
FTC=emtricitabine
GNB=gender non-binary
ISR=injection site reaction
LEN=lenacapavir
MACDP=Metropolitan Atlanta Congenital Defects Program
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
RBP=randomized blinded phase
SAE=serious adverse event
SUBQ=subcutaneous
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TGM=transgender men
TGW=transgender wome

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Yeztugo, Descovy, and Truvada US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.

YEZTUGO, DESCOVY, DESCOVY for PrEP, TRUVADA, TRUVADA for PrEP, GILEAD, and the GILEAD logo are registered trademarks of Gilead Sciences, Inc., or its related companies.
© 2026 Gilead Sciences, Inc.