GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Use in Pregnancy and Lactation

This document is in response to your request for clinical data on the use of Descovy for PrEP® (emtricitabine/tenofovir alafenamide [FTC/TAF] for HIV-1 pre-exposure prophylaxis [PrEP]) during pregnancy and lactation.

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 warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Summary

Product Labeling[1]

FTC/TAF is indicated in at-risk adults and adolescents weighing ≥35 kg for PrEP to reduce the risk of HIV-1 infection from sexual acquisition, excluding individuals at risk from receptive vaginal sex. Individuals must have a negative HIV-1 test immediately prior to initiating FTC/TAF for HIV-1 PrEP.

Limitations of Use: The indication does not include the use of FTC/TAF in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

Clinical Data on the Use of FTC/TAF During Pregnancy

PURPOSE 1 is an ongoing, phase 3, randomized, double-blind, 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: 218 pregnancies in the FTC/TAF group, 193 in the LEN group, and 98 in the FTC/TDF group.[3]
- Overall, 10 congenital abnormalities were reported, and study authors determined that the incidence was within the expected background rate and was balanced across all three treatment groups.[3]
- HIV acquisition occurred in 4 pregnant participants in the FTC/TAF group, in 1 pregnant participant in the FTC/TDF group, and in no pregnant participants in the LEN group.[3]

Available data from the APR showed no statistically significant difference in the overall risk of major birth defects for FTC or TAF compared with the background rate for major birth defects of 2.72% in a US reference population of the MACDP.[4]

Clinical Data on the Use of FTC/TAF During Lactation

Based on limited data, FTC has been shown to be present in human breast milk; it is not known if TAF is present in human breast milk.[1]

Clinical Data on the Use of FTC/TAF During Pregnancy

PURPOSE 1

Study design[2]

PURPOSE 1 (NCT04994509) is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TAF for HIV-1 PrEP in >5300 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. Study participants were randomized in a 2:2:1 ratio to LEN, FTC/TAF, and FTC/TDF, respectively. Randomly assigned participants were seen for follow-up at Weeks 4, 8, and 13 and at every 13 weeks thereafter. A planned interim analysis occurred when 50% of the randomly assigned participants had completed at least 52 weeks of follow-up.

Key inclusion criteria in the randomized phase of the study included: negative fourth generation HIV-1 Ab/Ag test confirmed with central HIV-1 testing, eGFR ≥60 mL/min at screening, and body weight ≥35 kg. Individuals were excluded if they had prior use of long-acting systemic HIV PrEP or HIV post-exposure prophylaxis.[5]

Participants who became pregnant could choose to remain in the trial and continue the trial drug after a new informed-consent process reviewing the benefits and risks.

Pregnancy outcomes[3]

At the data cutoff of May 8, 2024, there were 509 pregnancies among 487 participants: 218 pregnancies in the FTC/TAF group, 193 in the LEN group, and 98 in the FTC/TDF group (Table 1).

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). The study authors determined that the incidence of congenital abnormalities was within the expected background rate and was balanced across all three treatment groups.

Table 1. PURPOSE 1: Pregnancy Outcomes[3]

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

Pregnancy Outcomes, n or n (%)		FTC/TAF (n=208)	LEN (n=184)	FTC/TDF (n=95)
Pregnancy status	Completed	207 (95)	186 (96.4)	97 (99)
	Unknown	11 (5)	7 (3.6)	1 (1)
Live births[a]		119 (54.6)	128 (66.3)	56 (57.1)
Pregnancy losses		89 (40.8)	60 (31.1)	41 (41.8)
Stillbirth[b]		6 (2.8)	5 (2.6)	3 (3.1)
Induced abortion		50 (22.9)	35 (18.1)	23 (23.5)
Spontaneous miscarriage[c]		33 (15.1)	20 (10.4)	15 (15.3)

[a]Included data from 3 pregnancies that had 2 outcomes due to twins.
[b]Defined as occurring at ≥20 weeks' gestation.
[c]Defined as occurring at <20 weeks' gestation.

Among pregnant participants, HIV acquisition occurred in 4 participants in the FTC/TAF group, 1 participant in the FTC/TDF group, and in no participants in the LEN group. No cases of vertical transmission were observed.

Safety outcomes during pregnancy and postpartum are presented in Table 2.

Table 2. PURPOSE 1: Safety Outcomes During Pregnancy and Postpartum[3]

AEs During Pregnancy and Postpartum,[a] n (%)		FTC/TAF (n=208)	LEN (n=184)	FTC/TDF (n=95)
Any AEs		142 (68.3)	135 (73.4)	68 (71.6)
Grade ≥2		112 (53.8)	112 (60.9)	55 (57.9)
Grade ≥3		39 (18.8)	36 (19.6)	22 (23.2)
SAEs		50 (24)	41 (22.3)	22 (23.2)
AEs that led to study drug discontinuation		0	1 (0.5)[b]	0
AEs in ≥10% of participants in any group[c]	Urinary tract infection	34 (16.3)	39 (21.2)	27 (28.4)
	Vulvovaginal candidiasis	22 (10.6)	17 (9.2)	8 (8.4)
	Upper respiratory tract infection	16 (7.7)	20 (10.9)	6 (6.3)

Abbreviation: ISR=injection site reaction; SAE=serious adverse event.
[a]Included AEs that occurred during the randomized blinded phase from the last menstrual period date to 6 weeks after the pregnancy outcome date. ISRs related to study drug injections were excluded.
[b]Study drug discontinuation was due to spontaneous miscarriage.
[c]Spontaneous miscarriages were excluded.
Note: AEs were coded according to Medical Dictionary for Regulatory Activities (MedDRA) Version 27.1 and graded by the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1.

Antiretroviral Pregnancy Registry[4]

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.

FTC/TAF component data in the APR

The June 2025 interim report included prospective reports of 24,443 pregnancies with follow-up data through January 31, 2025. Birth defect prevalence by trimester of earliest exposure for all ARVs and FTC- and TAF-containing regimens is described in Table 3**.** For FTC and TAF, there are sufficient numbers of first-trimester exposures to detect at least a 1.5-fold increase in the risk of overall birth defects and a 2-fold increase in the risk of birth defects in the most common classes. No such increase has been detected to date.

The prevalence of pregnancies exposed to TAF in the first trimester was 4.06% (95% CI: 3.13–5.16%), which is significantly higher than the reports included in the CDC MACDP population-based birth defects surveillance system (2.72%; 95% CI: 2.68–2.76%) but not those included in the Texas Birth Defects Registry (4.66%; 95% CI: 4.64–4.67%). A detailed review of cases did not identify any pattern of birth defects related to TAF. The APR will continue to monitor TAF for any pattern of birth defects.

A full review of the available data evaluating TAF safety in pregnancy, including the APR, cases from Gilead's global safety database, published literature, and preclinical data, was conducted in January 2020; no association between TAF exposure and birth defects was found.[6]

Table 3. APR: Number of Birth Defects by Trimester of Earliest Exposure[4]

Drug Regimen	Pregnancies Enrolled, n	First Trimester		Second/Third Trimester	
		Defects per Live Births[a]	Prevalence % (95% CI)[b]	Defects per Live Births[a]	Prevalence % (95% CI)[b]
Any ARV-containing	24,443	382/12,853	3 (2.7, 3.3)	292/10,273	2.8 (2.5, 3.2)
FTC-containing	7939	165/5430	3 (2.6, 3.5)	56/2037	2.7 (2.1, 3.6)
TAF-containing	2044	63/1552	4.1 (3.1, 5.2)	16/394	4.1 (2.3, 6.5)

[a]Proportion of defects was calculated by dividing the number of defects that met the CDC criteria by the number of live births reported.

[b]Prevalence and 95% CIs were reported for drugs associated with ≥200 defect-positive live births, where the earliest exposure to drug was the first trimester.

Clinical Data on the Use of FTC/TAF During Lactation

Based on limited data, FTC has been shown to be present in human breast milk; it is not known if TAF is present in human breast milk. Studies in rats and monkeys have demonstrated that TFV is secreted in milk. TFV was excreted into the milk of lactating rats following oral administration of TDF (up to 600 mg/kg/day) at up to approximately 24% of the median plasma concentration in the highest dosed animals at lactation Day 11. TFV was excreted into the milk of lactating monkeys following a single subcutaneous (30 mg/kg) dose of TFV at concentrations up to approximately 4% of plasma concentration, resulting in exposure (AUC) of approximately 20% of plasma exposure.[1]

The safety of FTC/TAF for HIV-1 PrEP for infants exposed during lactation has not been adequately studied. Providers should discuss current evidence about the potential risks and

benefits of beginning or continuing PrEP during breastfeeding so that an informed decision can be made.

References

1. Enclosed. Gilead Sciences Inc, DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use. U. S. Prescribing Information. Foster City, CA.
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):1179-92.
3. 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]. 2025:
4. Antiretroviral Pregnancy Registry Steering Committee. *The Antiretroviral Pregnancy Registry Interim Report: 01 January 1989 Through 31 January 2025. Morrisville, NC*. 2025.
5. ClinicalTrials.gov. Study to Assess Safety and Efficacy of Lenacapavir and Emtricitabine/Tenofovir Alafenamide for Pre-Exposure Prophylaxis in Adolescent Girls and Young Women at Risk of HIV Infection (PURPOSE 1). ClinicalTrials.gov Identifier: NCT04994509. Available at: https://clinicaltrials.gov/ct2/show/NCT04994509?term=purpose-1&draw=2&rank=1. Accessed: 22 December. Last Updated: 19 December. 2022.
6. Gilead Sciences Inc. Data on File.

Abbreviations

Ab/Ag=antibody/antigen
AE=adverse event
APR=Antiretroviral Pregnancy Registry
ARV=antiretroviral
AUC=area under the concentration-time curve
CDC=Centers for Disease Control and Prevention
FTC=emtricitabine
LEN=lenacapavir
MACDP=Metropolitan Atlanta Congenital Defects Program
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV=tenofovir

Product Label

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

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