



**Recommendations for the Use of Antiretroviral Drugs in
Pregnant Women with HIV Infection and Interventions to Reduce
Perinatal HIV Transmission in the United States**

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Emtricitabine (Emtriva, FTC)

(Last updated December 7, 2018; last reviewed December 7, 2018)

Emtricitabine is classified as Food and Drug Administration Pregnancy Category B.

Animal Studies

Carcinogenicity

Emtricitabine was neither mutagenic nor clastogenic in a series of *in vitro* and animal *in vivo* screening tests. In long-term carcinogenicity studies of oral emtricitabine, no drug-related increases in tumor incidence were found in mice (at doses up to 26 times the human systemic exposure) or in rats (at doses up to 31 times the human systemic exposure) at the therapeutic dose.¹

Reproduction/Fertility

No effect of emtricitabine on reproduction or fertility was observed with doses that produced systemic drug exposures (as measured by area under the curve [AUC]) that were approximately 60-fold higher in female and male mice and 140-fold higher in male rats than human exposure at the recommended therapeutic dose.¹

Teratogenicity/Adverse Pregnancy Outcomes

No fetal variations or malformations were observed with emtricitabine dosing in mice that resulted in systemic drug exposure 60-fold higher than that observed in humans at recommended doses or in rabbits with dosing resulting in drug exposure 120-fold higher than human exposure.¹

Placental and Breast Milk Passage

Emtricitabine has been shown to cross the placenta in mice and rabbits; the average fetal/maternal drug concentration was 0.4 in mice and 0.5 in rabbits.²

Human Studies in Pregnancy

Pharmacokinetics

In the IMPAACT P1026s study, emtricitabine exposure was modestly lower during the third trimester (geometric mean 8.0 mcg*h/mL; 90% CI, 7.1–8.9) than during the postpartum period (9.7 mcg*h/mL; 90% CI, 8.6–10.9). Fifty-eight percent of pregnant women (15 of 26 women) versus 95% of postpartum women (21 of 22 women) met the AUC target ($\leq 30\%$ reduction from typical exposure for nonpregnant historical controls). Trough emtricitabine levels were also lower during pregnancy (C₂₄ geometric mean concentration [GMT] 58 ng/mL; 90% CI, 37–63) than during the postpartum period (C₂₄ GMT 85 ng/mL; 90% CI, 70–100).³ Similar differences in pharmacokinetic parameters of emtricitabine were found among women during pregnancy or after delivery in the PACTG 394 study⁴ and in a European study.^{5,6} The increase in emtricitabine clearance during pregnancy correlated with the normal pregnancy-related increase in glomerular filtration rate.⁶ These changes are not believed to be large enough to warrant dose adjustment during pregnancy.

Placental and Breast Milk Passage

Emtricitabine has been shown to have high placental transfer in pregnant women. In a study of 15 women who received emtricitabine during pregnancy, the mean cord-to-maternal-blood ratio was 1.2 (90% CI, 1.0–1.5).³ In eight women who were given a single dose of emtricitabine 600 mg with tenofovir disoproxil fumarate (TDF) 900 mg, the median cord blood emtricitabine concentration was 717 ng/mL (range 21–1,072), and the median cord blood/maternal plasma ratio was 0.85 (range 0.46–1.07).⁴

Emtricitabine is excreted into human milk. **Among women in Uganda and Nigeria who were taking first-line antiretroviral therapy that contained emtricitabine 200 mg, emtricitabine concentrations in breast milk peaked later than they did in maternal plasma (at 4–8 hours compared with 2–4 hours) and were three-fold higher than maternal plasma concentrations. Emtricitabine was detectable in three infants (19%).**⁷ In a study in the Ivory

Coast, five women with HIV who exclusively breastfed their newborn infants were given emtricitabine 400 mg, TDF 600 mg, and nevirapine 200 mg at onset of labor, followed by emtricitabine 200 mg and TDF 300 mg once daily for 7 days postpartum. The median minimal and maximal concentrations of emtricitabine in breast milk were 177 ng/mL and 679 ng/mL, respectively (interquartile ranges [IQR] 105–254 ng/mL and 658–743 ng/mL, respectively), well above the estimated emtricitabine IC₅₀ for HIV-1.⁸ In a study of 50 women without HIV who received 200 mg emtricitabine and 300 mg TDF orally daily as pre-exposure prophylaxis (PrEP), median peak and trough breast milk concentrations of emtricitabine were 212.5 ng/mL (IQR 140.0–405.0) and 183.0 ng/mL (IQR 113.0–250.0), respectively. Emtricitabine was detectable in 47 of 49 infants at a median (IQR) concentration of 13.2 ng/mL (9.3–16.7), corresponding to estimated daily infant ingestion of a 31.9-mcg/kg dose (IQR 21.0–60.8) of emtricitabine, or 0.5% of the daily dose for treating infants.⁹

Teratogenicity/Adverse Pregnancy Outcomes

A study of pregnancies conducted during an HIV PrEP trial randomized participants without HIV to receive placebo, TDF, or TDF plus emtricitabine. No increase in the incidence of congenital anomalies was observed in the TDF-plus-emtricitabine arm.¹⁰ There was no overall difference between the rate of pregnancy loss in the TDF-plus-emtricitabine arm and the rate of pregnancy loss in the TDF-alone arm of this PrEP study. In the U.S. PHACS/SMARTT cohort study, emtricitabine exposure was not associated with an increase in specific or overall birth defect risk.¹¹ In a large French cohort, emtricitabine exposure in the first trimester was associated with lower risk of birth defects.¹² In the Antiretroviral Pregnancy Registry, sufficient numbers of first-trimester exposures to emtricitabine in humans have been monitored to be able to detect at least a 1.5-fold increased risk of overall birth defects and a two-fold increase in cardiovascular and genitourinary defects (the most common classes). No such increase in birth defects has been observed with emtricitabine. Among cases of first-trimester emtricitabine exposure reported to the Antiretroviral Pregnancy Registry, the prevalence of birth defects was 2.44% (68 of 2,785 births; 95% CI, 1.90% to 3.09%), compared with a 2.72% total prevalence in the U.S. population, based on Centers for Disease Control and Prevention surveillance.¹³

Other Safety Information

In the U.S. PHACS/SMARTT cohort study, after adjusting for birth cohort and other factors, maternal use of emtricitabine led to no increase in the likelihood of adverse metabolic, growth and development, cardiac, neurological, or neurodevelopmental outcomes.¹⁴

Excerpt from Table 10^a

Note: When using FDCs, refer to other sections in Appendix B and Table 10 for information about the dosing and safety of individual drug components of the FDC during pregnancy.

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Use in Pregnancy
Emtricitabine (FTC) <i>Emtriva</i>	<u>FTC (Emtriva)</u> <u>Capsule:</u> • 200 mg	<u>Standard Adult Doses</u> <u>FTC (Emtriva)</u> <u>Capsule:</u> • 200 mg once daily without regard to food	High placental transfer to fetus. ^b
(FTC/TDF) <i>Truvada</i>	<u>Oral Solution:</u> • 10 mg/mL	<u>Oral Solution:</u> • 240 mg (24 mL) once daily without regard to food	No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects).
(FTC/EFV/TDF) <i>Atripla</i>	<u>FTC/TDF (Truvada):</u> • FTC 200 mg plus TDF 300 mg tablet	<u>FTC/TDF (Truvada):</u> • 1 tablet once daily without regard to food	If patient is HBV-coinfected, it is possible that a HBV flare may occur if the drug is stopped; see HIV/Hepatitis B Virus Coinfection .
(FTC/RPV/TDF) <i>Complera</i>	<u>FTC/EFV/TDF (Atripla):</u> • FTC 200 mg plus TDF 300 mg plus EFVc 600 mg tablet	<u>FTC/TDF/EFV (Atripla):</u> • 1 tablet once daily at or before bedtime	
(FTC/EVG/COBI/TDF) <i>Stribild</i>	<u>FTC/RPV/TDF (Complera):</u> • FTC 200 mg plus TDF 300 mg plus RPV 25 mg tablet	• Take on an empty stomach to reduce side effects.	
(FTC/TAF) <i>Descovy</i>	<u>FTC/EVG/COBI/TDF (Stribild):</u> • FTC 200 mg plus TDF 300 mg plus EVG 150 mg plus COBI 150 mg tablet	<u>FTC/TDF/RPV (Complera):</u> • 1 tablet once daily with food	
(FTC/RPV/TAF) <i>Odefsey</i>	<u>FTC/TAF (Descovy):</u> • FTC 200 mg plus TAF 25 mg tablet	<u>FTC/TDF/EFV/COBI (Stribild):</u> • 1 tablet once daily with food	
(FTC/EVG/COBI/TAF) <i>Genvoya</i>	<u>FTC/RPV/TAF (Odefsey):</u> • FTC 200 mg plus TAF 25 mg plus RPV 25 mg tablet	<u>FTC/TAF (Descovy):</u> • 1 tablet once daily with or without food	
(FTC/BIC/TAF) <i>Biktarvy</i>	<u>FTC/EVG/COBI/TAF (Genvoya):</u> • FTC 200 mg plus TAF 10 mg plus EVG 150 mg plus COBI 150 mg tablet	<u>FTC/TAF/RPV (Odefsey):</u> • 1 tablet once daily with food	
(FTC/DRV/COBI/TAF) <i>Symtuza</i>	<u>FTC/BIC/TAF (Biktarvy):</u> • FTC 200 mg plus TAF 25 mg plus BIC 50 mg tablet	<u>FTC/TAF/EVG/COBI (Genvoya):</u> • 1 tablet once daily with food	
	<u>FTC/DRV/COBI/TAF (Symtuza):</u> • DRV 800 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg tablet	<u>FTC/TAF/BIC (Biktarvy):</u> • 1 tablet once daily with or without food	
		<u>DRV/COBI/FTC/TAF (Symtuza):</u> • 1 tablet once daily with food	
		<u>Dosing in Pregnancy:</u> • No change in FTC dose indicated.	
		<u>PK in Pregnancy:</u> • PK of FTC is not significantly altered in pregnancy.	
		• For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., TDF, TAF, EFV, RPV, DRV, EVG, BIC, COBI)	

^a Individual ARV drug dosages may need to be adjusted in patients with renal or hepatic insufficiency (for details, see the [Adult and Adolescent Guidelines, Appendix B, Table 8](#)).

^b Placental transfer categories are determined by mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6 **Moderate:** 0.3–0.6 **Low:** <0.3

Key to Acronyms: BIC = bicitgravir; COBI = cobicistat; DRV = darunavir; EFV = efavirenz; EVG = elvitegravir; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; PK = pharmacokinetic; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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