

Emtricitabine (Emtriva, FTC)

(Last updated June 7, 2016; last reviewed June 7, 2016)

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]) 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/Developmental Toxicity

Incidence of fetal variations and malformations was not increased with emtricitabine dosing in mice that resulted in systemic drug exposure 60-fold higher than observed with human exposure 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

Emtricitabine pharmacokinetic (PK) parameters have been evaluated in 18 HIV-infected pregnant women receiving antiretroviral therapy including emtricitabine (200 mg once daily) at 30 to 36 weeks' gestation and 6 to 12 weeks postpartum.³ Emtricitabine exposure was modestly lower during the third trimester (8.6 mcg*h/mL [5.2–15.9]) compared with the postpartum period (9.8 mcg*h/mL [7.4–30.3]). Two-thirds (12 of 18) of pregnant women versus 100% (14 of 14) of postpartum women met the AUC target (10th percentile in non-pregnant adults). Trough emtricitabine levels were also lower during pregnancy (minimum plasma concentration 52 ng/mL [14–180]) compared with the postpartum period (86 ng/mL [<10 to 306]). In the IMPAACT P1026s study, similar **alterations were seen, but the** 24-hour, post-dose levels were well above the inhibitory concentration 50% (IC₅₀) in all patients.⁴ Similar differences in PK parameters of emtricitabine among women during pregnancy or after delivery were found in the PACTG 394 study⁵ and in a European study.^{6,7} The increase in emtricitabine clearance in pregnancy correlated with the normal pregnancy-related increase in glomerular filtration rate.⁷ These changes are not believed to be large enough to warrant dosage adjustment during pregnancy.

Placental and Breast Milk Passage

Emtricitabine has been shown to have high placental transfer in pregnant women. In 18 women who received 200 mg emtricitabine once daily during pregnancy, mean cord blood concentration was 300 ± 268 ng/mL and the mean ratio of cord blood/maternal emtricitabine concentrations was 1.17 ± 0.6 (n = 9).³ In a study of 15 women who received emtricitabine during pregnancy, the mean cord-to-maternal-blood ratio was 1.2 (90% confidence interval [CI], 1.0–1.5).⁴ In 8 women who were given a single dose of 600 mg emtricitabine with 900 mg tenofovir disoproxil fumarate (TDF), the median cord blood emtricitabine concentration was 717 ng/mL (range 21–1,072), and the median cord blood/maternal ratio was 0.85 (range 0.46–1.07).⁵

Emtricitabine is excreted into human milk. In a study in the Ivory Coast, 5 HIV-infected women who exclusively breastfed their newborn infants were given 400 mg emtricitabine, 600 mg TDF, and 200 mg

nevirapine at onset of labor, followed by 200 mg emtricitabine and 300 mg TDF once daily for 7 days postpartum. The median minimal and maximal concentrations of emtricitabine in breast milk were 177 and 679 ng/mL, respectively (interquartile ranges 105–254 and 658–743 ng/mL, respectively), well above the estimated emtricitabine IC₅₀ for HIV-1.⁸

Teratogenicity/Developmental Toxicity

In a study of pregnancies occurring during an HIV pre-exposure prophylaxis (PrEP) trial in which HIV-uninfected participants were randomized to placebo, TDF, or TDF plus emtricitabine, there was no increase in congenital anomalies in the TDF-plus-emtricitabine arm.⁹ There was no overall difference in the rate of pregnancy loss in the TDF-plus-emtricitabine or TDF-alone arms of this PrEP study. In a large French cohort, emtricitabine exposure in the first trimester was associated with lower risk of birth defects.¹⁰ In the Antiretroviral Pregnancy Registry (APR), 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 2-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 APR, the prevalence of birth defects was **2.4% (47 of 1,984 births; 95% CI, 1.7% to 3.1%)**, compared with a 2.7% total prevalence in the U.S. population, based on Centers for Disease Control and Prevention surveillance.¹¹

Excerpt from Table 8^a (page 1 of 2)

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Use in Pregnancy
Emtricitabine (FTC) <i>Emtriva</i>	<u>Emtriva (FTC)</u> <i>Capsules:</i> • 200 mg	<u>Standard Adult Dose(s)</u> <i>Emtriva (FTC)</i> <i>Capsule:</i> • 200 mg once daily without regard to food	High placental transfer to fetus. ^b
(FTC/TDF) <i>Truvada</i>	<i>Oral Solution:</i> • 10 mg/mL	<i>Oral Solution:</i> • 240 mg (24 mL) once daily without regard to food	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects).
(FTC/TDF/EFV) <i>Atripla</i>	<u>Truvada:</u> • FTC 200 mg plus TDF 300 mg tablet	<u>Truvada:</u> • 1 tablet once daily without regard to food	If HBV-coinfected, it is possible that a HBV flare may occur if the drug is stopped; see HIV/Hepatitis B Virus Coinfection .
(FTC/TDF/RPV) <i>Complera</i>	<u>Atripla:</u> • FTC 200 mg plus TDF 300 mg plus EFV ^c 600 mg tablet	<u>Atripla:</u> • 1 tablet once daily at or before bedtime. Take on an empty stomach to reduce side effects.	
(FTC/TAF/RPV) <i>Odefsey</i>	<u>Complera:</u> • FTC 200 mg plus TDF 300 mg plus RPV 25 mg tablet	<u>Complera:</u> • 1 tablet once daily with food	
(FTC/TAF/EVG/COBI) <i>Genvoya</i>	<u>Stribild:</u> • FTC 200 mg plus TDF 300 mg plus EVG 150 mg plus COBI 150 mg tablet	<u>Stribild:</u> • 1 tablet once daily with food	
	<u>Odefsey:</u> • FTC 200 mg plus TAF 25 mg plus RPV 25 mg tablet	<u>Odefsey:</u> • 1 tablet once daily with food	
	<u>Genvoya:</u> • FTC 200 mg plus TAF 10 mg plus EVG 150 mg plus COBI 150 mg tablet	<u>Genvoya:</u> • 1 tablet once daily with food	
		<u>PK in Pregnancy:</u> • PK of FTC not significantly altered in pregnancy.	
		<u>Dosing in Pregnancy:</u> • No change in FTC dose indicated.	

Excerpt from Table 8^a (page 2 of 2)

^a Individual antiretroviral drug dosages may need to be adjusted in renal or hepatic insufficiency (for details, see [Adult Guidelines, Appendix B, Table 7](#)).

^b Placental transfer categories—Mean or median cord blood/maternal delivery plasma drug ratio:

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

^c See [Teratogenicity](#) for discussion of EFV and risks in pregnancy.

Key to Acronyms: COBI = cobicistat; EFV = efavirenz; FTC = emtricitabine; HBV = hepatitis B virus; PK = pharmacokinetic; RPV = rilpivirine; TDF = tenofovir disoproxil fumarate

References

1. Emtricitabine (Emtriva) [package insert]. Food and Drug Administration. 2012. Available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021500s0191bl.pdf. Accessed April 6, 2016.
2. Szczech GM, Wang LH, Walsh JP, Rousseau FS. Reproductive toxicology profile of emtricitabine in mice and rabbits. *Reprod Toxicol*. 2003;17(1):95-108. Available at <http://www.ncbi.nlm.nih.gov/pubmed/12507664>.
3. Hirt D, Urien S, Rey E, et al. Population pharmacokinetics of emtricitabine in human immunodeficiency virus type 1-infected pregnant women and their neonates. *Antimicrob Agents Chemother*. 2009;53(3):1067-1073. Available at <http://www.ncbi.nlm.nih.gov/pubmed/19104016>.
4. Stek AM, Best BM, Luo W, et al. Effect of pregnancy on emtricitabine pharmacokinetics. *HIV Med*. 2012;13(4):226-235. Available at <http://www.ncbi.nlm.nih.gov/pubmed/22129166>.
5. Flynn PM, Mirochnick M, Shapiro DE, et al. Pharmacokinetics and safety of single-dose tenofovir disoproxil fumarate and emtricitabine in HIV-1-infected pregnant women and their infants. *Antimicrob Agents Chemother*. 2011;55(12):5914-5922. Available at <http://www.ncbi.nlm.nih.gov/pubmed/21896911>.
6. Colbers AP, Hawkins DA, Gengelmaier A, et al. The pharmacokinetics, safety and efficacy of tenofovir and emtricitabine in HIV-1-infected pregnant women. *AIDS*. 2013;27(5):739-748. Available at <http://www.ncbi.nlm.nih.gov/pubmed/23169329>.
7. Valade E, Treluyer JM, Dabis F, et al. Modified renal function in pregnancy: impact on emtricitabine pharmacokinetics. *Br J Clin Pharmacol*. 2014;78(6):1378-1386. Available at <http://www.ncbi.nlm.nih.gov/pubmed/24995851>.
8. Benaboud S, Pruvost A, Coffie PA, et al. Concentrations of tenofovir and emtricitabine in breast milk of HIV-1-infected women in Abidjan, Cote d'Ivoire, in the ANRS 12109 TEmAA Study, Step 2. *Antimicrob Agents Chemother*. 2011;55(3):1315-1317. Available at <http://www.ncbi.nlm.nih.gov/pubmed/21173182>.
9. Mugo NR, Hong T, Celum C, et al. Pregnancy incidence and outcomes among women receiving preexposure prophylaxis for HIV prevention: a randomized clinical trial. *JAMA*. 2014;312(4):362-371. Available at <http://www.ncbi.nlm.nih.gov/pubmed/25038355>.
10. Sibiude J, Mandelbrot L, Blanche S, et al. Association between prenatal exposure to antiretroviral therapy and birth defects: an analysis of the French perinatal cohort study (ANRS CO1/CO11). *PLoS Med*. 2014;11(4):e1001635. Available at <http://www.ncbi.nlm.nih.gov/pubmed/24781315>.
11. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 Jan 1989–31 July 2015. Wilmington, NC: Registry Coordinating Center. 2015. Available at <http://www.apregistry.com/>.