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 November 14, 2017; last reviewed November 14, 2017)*

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/Adverse Pregnancy Outcomes**

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**

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]) compared with the postpartum period (9.7 mcg*h/mL [90% CI, 8.6–10.9]). Fifty-eight percent (15 of 26) of pregnant women versus 95% (21 of 22) of postpartum women met the AUC target (<30% reduction from typical exposure for nonpregnant historical controls). Trough emtricitabine levels were also lower during pregnancy (C24 geometric mean concentration 58 ng/mL [90% CI, 37–63]) compared with the postpartum period (85 ng/mL [90% CI, 70–100]).³ Similar differences in pharmacokinetic parameters of emtricitabine among women during pregnancy or after delivery were found in the PACTG 394 study⁴ and in a European study.⁵,⁶ The increase in emtricitabine clearance in pregnancy correlated with the normal pregnancy-related increase in glomerular filtration rate.⁶ 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 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 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).⁴

Emtricitabine is excreted into human milk. In a study in the Ivory Coast, 5 women with HIV 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 IC$_{50}$ for HIV-1. 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 breastmilk concentrations of emtricitabine were 212.5 ng/mL (IQR 140.0–405.0) and 183.0 ng/mL (113.0–250.0), respectively. Emtricitabine was detectable in 47/49 infants at a median (IQR) concentration of 13.2 ng/mL (9.3-16.7), corresponding to estimated daily infant ingestion of 31.9 mcg/kg (IQR 21.0-60.8) dose of emtricitabine, or 0.5% of the daily dose for treating infants.8

Teratogenicity/Adverse Pregnancy Outcomes

In a study of pregnancies occurring during an HIV PrEP trial in which participants (who did not have HIV infection) 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 the U.S. PHACS SMARTT cohort study, emtricitabine exposure was not associated with an increase in specific or overall birth defect risk.10 In a large French cohort, emtricitabine exposure in the first trimester was associated with lower risk of birth defects.11 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 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 2.24% (48 of 2,145 births; 95% CI, 1.65% to 2.96%), compared with a 2.72% total prevalence in the U.S. population, based on Centers for Disease Control and Prevention surveillance.12

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/development, cardiac, neurological, or neurodevelopmental outcomes.13
Excerpt from Table 9

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulation</th>
<th>Dosing Recommendations</th>
<th>Use in Pregnancy</th>
</tr>
</thead>
</table>
| Emtricitabine (FTC) Emtriva           | Capsules: 200 mg | Standard Adult Dose Emtriva (FTC) Capsule: 200 mg once daily without regard to food | High placental transfer to fetus. 
No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). |
| (FTC/TDF) Truvada                    | Oral Solution: 10 mg/mL | Truvada: 240 mg (24 mL) 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/EFV) Atripla                | Truvada: FTC 200 mg plus TDF 300 mg tablet | Atripla: 1 tablet once daily without regard to food | |
| (FTC/TDF/RPV) Complera               | Atripla: FTC 200 mg plus TDF 300 mg plus EFV<sub>c</sub> 600 mg tablet | Complera: 1 tablet once daily at or before bedtime. Take on an empty stomach to reduce side effects. | |
| (FTC/TAF) Stribild                   | Complera: FTC 200 mg plus TDF 300 mg plus RPV 25 mg tablet | Stribild: 1 tablet once daily with food | |
| (FTC/TAF/RPV) Odefsey                | Stribild: FTC 200 mg plus TDF 300 mg plus EVG 150 mg plus COBI 150 mg tablet | Odefsey: 1 tablet once daily with food | |
| (FTC/TAF/EVG/COBI) Descovy            | Descovy: FTC 200 mg plus TAF 25 mg | Descovy: 1 tablet once daily with or without food | |
| (FTC/TAF/RPV) Genvoya                | Odefsey: FTC 200 mg plus TAF 25 mg plus RPV 25 mg tablet | Genvoya: 1 tablet once daily with food | |
|                                        | Genvoya: FTC 200 mg plus TAF 10 mg plus EVG 150 mg plus COBI 150 mg tablet | PK in Pregnancy: PK of FTC not significantly altered in pregnancy. | |

References


