



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Maraviroc (Selzentry, MVC)

(Last updated October 26, 2016; last reviewed October 26, 2016)

Maraviroc is classified as Food and Drug Administration Pregnancy Category B.!

Animal Studies

Carcinogenicity

Maraviroc was neither mutagenic nor clastogenic in a series of *in vitro* and animal *in vivo* screening tests. Long-term animal carcinogenicity studies of maraviroc showed no drug-related increases in tumor incidence.

Reproduction/Fertility

Reproductive toxicity has been evaluated in rats and rabbits. Maraviroc produced no adverse effects on fertility of male or female rats at doses with exposures (area under the curve [AUC]) up to 20-fold higher than in humans given the recommended 300-mg, twice-daily dose.

Teratogenicity/Developmental Toxicity

The incidence of fetal variations and malformations was not increased in embryo-fetal toxicity studies in rats at AUC approximately 20-fold higher (and in rabbits at approximately 5-fold higher) than human exposures at the recommended 300-mg, twice-daily dose (up to 1000 mg/kg/day in rats and 75 mg/kg/day in rabbits).

Placental and Breast Milk Passage

Minimal placental passage was demonstrated in a study of single-dose maraviroc in rhesus macaques that showed poor placental transfer and rapid clearance from infant monkeys' blood.² Studies in lactating rats indicate that maraviroc is extensively secreted into rat milk.!

Human Studies in Pregnancy

Pharmacokinetics

A U.S./European study of intensive, steady-state 12-hour pharmacokinetic profiles in the third trimester and at least 2 weeks postpartum included 18 women taking maraviroc as part of clinical care.³ Sixty-seven percent were taking 150 mg BID with a protease inhibitor; 11% took 300 mg BID and 22% took an alternative regimen. The geometric mean ratios for third-trimester versus postpartum AUC were 0.72 and 0.70 for maximum maraviroc concentration. Despite the overall 30% decrease in maraviroc exposure during pregnancy and 15% decrease in C_{trough} , C_{trough} exceeded the minimum target concentration of 50 ng/mL, and only one woman had a C_{trough} below that level both during pregnancy and post-partum. These data suggest that the standard adult dose adjusted for concomitant antiretroviral (ARV) drugs seems appropriate in pregnancy. A review of drug interactions between ARV drugs and oral contraceptives found that it is safe to coadminister oral contraceptives with maraviroc.⁴

Other Safety Issues

A retrospective study from an English-Irish cohort of 857 pregnant women showed an increased rate of hepatotoxicity among the 492 who started antiretroviral therapy during pregnancy.⁵ Maraviroc was one of three drugs that was associated with an increased risk of liver enzyme elevation during pregnancy with an aHR of 4.19 [1.34–13.1, $P = 0.01$], along with efavirenz and nevirapine. In a model using human placental BeWo cells, maraviroc inhibited transplacental passage of two fluorescent organic cations, suggesting that it might influence placental drug transfer and cause drug-drug interactions.⁶

Placental and Breast Milk Passage

An *ex vivo* human placental cotyledon perfusion model demonstrated minimal placental passage of maraviroc.⁷ In a study in humans of 6 mother/infant pairs, the median ratio of cord blood-to-maternal-plasma drug concentrations was 0.33 (0.03–0.56).!⁸ Whether maraviroc is secreted into human milk is unknown.

Teratogenicity/Developmental Toxicity

In the Antiretroviral Pregnancy Registry, insufficient numbers of first-trimester exposures to maraviroc in

humans have been monitored to be able to make a risk determination.^{9,10}

Excerpt from Table 8^a

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Use in Pregnancy
Maraviroc (MVC) Selzentry	Tablets: • 150 mg • 300 mg	<p><u>Standard Adult Dose:</u></p> <ul style="list-style-type: none"> • 300 mg twice daily with or without food • MVC must be used in combination with other ARVs in HIV-1-infected adults with only CCR5-tropic virus. <p><u>Dose Adjustments:</u></p> <ul style="list-style-type: none"> • Increase to 600 mg BID when used with potent CYP3A inducers: EFV, ETR, and rifampin. • Decrease to 150 mg BID when used with CYP3A inhibitors: all PIs except TPV/r and itraconazole. <p><u>PK in Pregnancy:</u></p> <ul style="list-style-type: none"> • A PK study in human pregnancy demonstrated a 20% to 30% overall decrease in AUC, but C_{trough} exceeded the recommended minimal concentration of 50 ng/mL. <p><u>Dosing in Pregnancy:</u></p> <ul style="list-style-type: none"> • Standard adult dosing adjusted for concomitant ARV use appears appropriate. 	<p>No evidence of teratogenicity in rats or rabbits; insufficient data to assess for teratogenicity in humans.</p> <p>MVC placental passage category should be moderate.^b</p>

^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:

Key to Abbreviations: ARV = antiretroviral; AUC = area under the curve; BID = twice daily; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; PI = protease inhibitor; PK = pharmacokinetic

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