



**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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Nevirapine (Viramune, NVP)

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Available data from the Antiretroviral Pregnancy Registry show no difference between the risk of overall major birth defects for nevirapine and the background rate for major birth defects in a U.S. reference population.

Animal Studies

Carcinogenicity

Nevirapine showed no evidence of mutagenic or clastogenic activity in a battery of *in vitro* and *in vivo* studies. The occurrence of hepatocellular adenomas and carcinomas increased at all doses in male mice and rats and at higher doses in female mice and rats. Systemic exposure at all studied doses was lower than systemic exposure in humans receiving therapeutic nevirapine doses. Given the lack of genotoxic activity of nevirapine, the relevance to humans of hepatocellular neoplasms in nevirapine-treated mice and rats is unknown.¹

Reproduction/Fertility

Evidence of impaired fertility was seen in female rats receiving nevirapine doses that produced systemic exposures comparable to human therapeutic exposure.¹

Teratogenicity/Adverse Pregnancy Outcomes

In reproductive studies of rats and rabbits, teratogenic effects of nevirapine have not been observed at systemic exposures approximately equivalent to or 50% greater than the recommended human dose (based on area under the curve [AUC]). In pregnant rats, however, a significant decrease in fetal weight occurred at doses that produced systemic concentrations approximately 50% higher than human therapeutic exposure.¹

Human Studies in Pregnancy

Pharmacokinetics

The pharmacokinetics (PKs) of nevirapine have been evaluated in pregnant women who received nevirapine as part of antiretroviral therapy (ART) during pregnancy. A study that determined nevirapine PKs in 26 women during pregnancy (which included seven women in their second trimester and 19 women in their third trimester) and again in the same women 4 to 12 weeks after delivery found that pregnancy did not alter nevirapine PK parameters.² In contrast, nevirapine clearance was 20% greater, AUC was 28% lower, and maximum plasma concentration was 30% lower in 16 pregnant women than in 13 nonpregnant women, based on nevirapine PK data from a therapeutic drug monitoring program that included 12-hour sampling; the authors of that study also reported high variability in plasma nevirapine concentrations.³ A Dutch study reported a nonsignificant trend toward lower nevirapine exposure during pregnancy, with steady-state nevirapine concentrations of 5.2 mcg/mL in 45 pregnant women compared to 5.8 mcg/mL in 152 nonpregnant women ($P = 0.08$).⁴ An intensive PK study of 59 women with genotype information found that pregnant women who had one or two mutations in CYP2B6 had higher nevirapine clearance than a different group of postpartum women who had one or two mutations in CYP2B6.⁵ In fast metabolizers (no mutations), no differences in nevirapine exposure were seen between pregnant women and postpartum women. No dose adjustment during pregnancy is currently recommended for nevirapine.

Placental and Breast Milk Passage

Nevirapine demonstrates rapid and effective placental transfer, achieving near equivalent concentrations in maternal and cord blood (cord-to-maternal-blood ratio ranges from 0.60–1.02).^{6,7} Nevirapine has also been shown to be excreted into human breast milk. In a study of 57 Malawian women who received postpartum nevirapine-based therapy, the breast-milk-to-maternal-serum concentration ratio was approximately 0.6; detectable nevirapine concentrations were found in the breastfeeding infants (interquartile range 0.54–1.06 mcg/mL).⁸ In data from 15 breastfeeding women who received nevirapine-based therapy in Botswana,

median maternal plasma concentration at 1 month postpartum was 6.71 mcg/mL and median maternal breast milk concentration was 1.83 mcg/mL, for a median maternal breast-milk-to-plasma ratio of 0.27.⁹ Infant exposure was measured at 1 month in nine infants; all infants had biologically significant, detectable nevirapine concentrations in their blood, with a median level of 0.37 mcg/mL (and a range of 0.24–1.2 mcg/mL), representing approximately 6% of median maternal value. Similar data were reported in a study of 67 mothers who received nevirapine-based therapy in Kenya; the median concentration of nevirapine in breast milk was 4.55 mcg/mL, with median concentrations in breastfeeding infants of 0.99 mcg/mL, 1.03 mcg/mL, and 0.73 mcg/mL at 2, 6, and 14 weeks postpartum, respectively.¹⁰ An additional study in 122 Nigerian mother/infant pairs found that the median milk-to-plasma nevirapine AUC ratio was 0.95 (with a range of 0.56–1.5). Infant plasma concentrations from exposure through breast milk were 660 ng/mL (with a range of 104–3,090 ng/mL).⁵

Teratogenicity/Adverse Pregnancy Outcomes

In the Antiretroviral Pregnancy Registry, sufficient numbers of first-trimester exposures to nevirapine in humans have been monitored to be able to detect at least a 1.5-fold increase in 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 nevirapine. Among cases of first-trimester nevirapine exposure reported to the Antiretroviral Pregnancy Registry, the prevalence of birth defects was 2.80% (32 of 1,142 births; 95% CI, 1.92% to 3.93%) compared with a total prevalence of 2.72% in the U.S. population, based on Centers for Disease Control and Prevention surveillance.¹¹ Similarly, the French Perinatal Cohort reported no association between nevirapine and birth defects with 71% power to detect a 1.5-fold increase.¹²

Safety

Severe, life-threatening, and (in some cases) fatal hepatotoxicity—including fulminant and cholestatic hepatitis, hepatic necrosis, hepatic failure, and severe, life-threatening hypersensitivity skin reactions, including Stevens-Johnson syndrome—has been reported in patients with HIV receiving nevirapine in combination with other drugs for treatment of HIV disease and in a small number of individuals receiving nevirapine as part of ART for postexposure prophylaxis of nosocomial or sexual exposure to HIV.¹³ In general, in controlled clinical trials, clinical hepatic events, regardless of severity, occurred in 4.0% of patients (with a range of 0% to 11.0%) who received nevirapine; however, the risk of nevirapine-associated liver failure or hepatic mortality has been lower, ranging from 0.04% to 0.40%.^{1,14} The greatest risk of severe rash or hepatic events occurs during the first 6 to 18 weeks of therapy, although the risk of toxicity continues past this period and monitoring should continue at frequent intervals.

Incidence of severe nevirapine-associated skin rash has been reported to be 5.5 times to 7.3 times more common in women than men and cases have been reported in pregnant women.¹⁵⁻¹⁷ Other studies have found that hepatic adverse events with systemic symptoms (often rash) were 3.2-fold more common in women than men.¹⁴ Several studies suggest that the degree of risk of hepatic toxicity varies with CD4 T lymphocyte (CD4) cell count. In a summary analysis of data from 17 clinical trials of nevirapine therapy, women with CD4 cell counts >250 cells/mm³ were 9.8 times more likely to experience symptomatic, often rash-associated, nevirapine-related hepatotoxicity than women with lower CD4 cell counts.¹⁴ Higher CD4 cell counts have also been associated with increased risk of severe nevirapine-associated skin rash.¹⁶ Rates of hepatotoxicity and rash similar to those in U.S. studies have been seen in international cohorts of nonpregnant women, although not all studies have reported an association between rates of hepatotoxicity and rash and CD4 cell counts >250 cells/mm³.¹⁸ In a study of 359 nonpregnant women randomized to receive nevirapine-based therapy in sub-Saharan Africa, higher nevirapine exposure was associated with development of severe skin toxicity, and baseline CD4 cell counts ≥250 cells/mm³ were associated with nevirapine-related liver toxicity and drug discontinuation.¹⁹ Some researchers have suggested that genetic variation in drug metabolism polymorphisms (e.g., CYP2B6 variants), TRAF proteins, and immune human leukocyte antigen loci may be associated with higher risk of nevirapine-associated adverse events and that the relationship between genetic variants and adverse events may vary by race.²⁰⁻²³ Published literature indicates that rash and hyperbilirubinemia have been seen in infants exposed to nevirapine through breastmilk.¹

Although fatal cases of hepatic failure have been reported in pregnant women with HIV who were receiving nevirapine as part of an ART regimen, it is uncertain whether pregnancy increases the risk of hepatotoxicity in women receiving nevirapine or other antiretroviral drugs.²⁴ In a systematic review of 20 studies that included 3,582 pregnant women from 14 countries, the pooled proportion of women experiencing a severe hepatotoxic event was 3.6% (95% CI, 2.4% to 4.8%) and the proportion of women experiencing severe rash was 3.3% (95% CI, 2.1% to 4.5%); overall, 6.2% of women stopped nevirapine due to an adverse event (95% CI, 4.0% to 8.4%).²⁵ These results were comparable to published frequencies in the general adult population and comparable to frequencies in nonpregnant women within the same cohorts. These data suggest that the frequency of adverse events associated with nevirapine during pregnancy is not higher than the frequency reported for nevirapine in the general population, consistent with data from two multicenter prospective cohorts in which pregnancy was not associated with an increased risk of nevirapine-associated hepatic toxicity.^{26,27} In contrast, an analysis of data collected in the United Kingdom and Ireland from 2000 to 2011 evaluated 3,426 women, one-quarter of whom were pregnant, and found that pregnant women taking efavirenz, maraviroc, or nevirapine were at increased risk of liver enzyme elevation.²⁸

In the systematic review discussed above, there was a nonsignificant trend toward an increased likelihood of cutaneous events (odds ratio [OR] 1.1; 95% CI, 0.8–1.6) and severe cutaneous adverse events in pregnant women with CD4 cell counts ≥ 250 cell/mm³ (OR 1.4, 95% CI, 0.8–2.4).²⁵ A separate systematic review of 14 studies did report a significant association between increased toxicity risk and initiation of nevirapine-based therapy during pregnancy in women with CD4 cell counts ≥ 250 cells/mm³.²⁹ A small case-control study (6 cases, 30 controls) in South Africa reported that pregnancy increased the chance of developing Stevens-Johnson syndrome (OR 14.28, $P = 0.006$; 95% CI, 1.54–131.82).³⁰ Nevirapine (as a component of a combination regimen) should be initiated in pregnant women with CD4 cell counts ≥ 250 cells/mm³ only if the benefit clearly outweighs the risk. Women with CD4 cell counts < 250 cells/mm³ can receive nevirapine-based regimens, and women who become pregnant while taking nevirapine and who are tolerating their regimens well can continue therapy, regardless of CD4 cell count.

In a chart abstraction study that used data collected at eight government hospitals in Botswana, women receiving ART regimens that contained nevirapine were more likely to experience certain adverse events than women on ART regimens that did not contain nevirapine, including hypertension (30% vs. 16%), severe hypertension (3.3% vs. 1.2%), gestational hypertension (18% vs. 10%), and early gestational hypertension (12% vs. 7%).³¹

Because pregnancy itself can mimic some of the early symptoms of hepatotoxicity (i.e., pregnancy-related nausea and vomiting), health care providers who are caring for women receiving nevirapine during pregnancy should be aware of this potential complication. Frequent and careful monitoring of clinical symptoms and hepatic transaminases (i.e., alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) is necessary, particularly during the first 18 weeks of therapy. Some clinicians measure serum transaminases at baseline, every 2 weeks for the first month, and then monthly for the first 18 weeks; in patients with pre-existing liver disease, monitoring should be performed more frequently when initiating therapy and monthly thereafter.³² Transaminase levels should be checked in all women who develop a rash while receiving nevirapine. Patients who develop suggestive clinical symptoms accompanied by elevation in serum transaminase levels (ALT and/or AST) or who have asymptomatic but severe transaminase elevations should stop nevirapine and not receive the drug in the future.

Additional Information

In a nonrandomized parallel-group study of etonogestrel exposure in women who were taking concomitant ART, nevirapine had no effect on etonogestrel levels, in contrast to efavirenz.³³

Excerpt from Table 10^a

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Use in Pregnancy
Nevirapine (NVP) Viramune Viramune XR (Extended Release) Note: Generics are available for some formulations	<u>NVP (Viramune)</u> Tablets: • 200 mg ^d Oral Suspension: • 50 mg/5 mL <u>Viramune XR</u> Tablets: • 100 mg ^d • 400 mg ^d	<u>Standard Adult Dose:</u> • 200 mg once-daily Viramune (immediate release) for 14 days (lead-in period); thereafter, 200 mg twice daily or 400 mg (Viramune XR tablet) once daily, without regard to food. • Repeat lead-in period if therapy is discontinued for >7 days. • In patients who develop mild-to-moderate rash without constitutional symptoms during lead-in period, continue lead-in dosing until rash resolves, but administer for ≤28 days total. <u>PK in Pregnancy:</u> • PK of immediate release tablets is not significantly altered in pregnancy. • No data are available on extended release formulations in pregnancy. <u>Dosing in Pregnancy:</u> • No change in dose indicated.	High placental transfer to fetus. ^b No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects and 2-fold increase in cardiovascular and genitourinary defects. Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 cell counts ≥250/mm ³ when first initiating therapy; pregnancy does not appear to increase risk. NVP should be initiated in pregnant women with CD4 cell counts ≥250 cells/mm ³ only if benefit clearly outweighs risk because of potential increased risk of life-threatening hepatotoxicity in women with high CD4 cell counts. Elevated transaminase levels at baseline may increase the risk of NVP toxicity. Women who become pregnant while taking NVP-containing regimens and who are tolerating their regimens well can continue therapy, regardless of CD4 cell count.

^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

^d Generic formulation available

Key to Acronyms: ARV = antiretroviral; CD4 = CD4 T lymphocyte; NVP = nevirapine; PK = pharmacokinetic

References

1. Nevirapine [package insert]. Food and Drug Administration. 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020636s048,020933s0381bl.pdf.
2. Capparelli EV, Aweeka F, Hitti J, et al. Chronic administration of nevirapine during pregnancy: impact of pregnancy on pharmacokinetics. *HIV Med.* 2008;9(4):214-220. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18366444>.
3. von Hentig N, Carlebach A, Gute P, et al. A comparison of the steady-state pharmacokinetics of nevirapine in men, nonpregnant women and women in late pregnancy. *Br J Clin Pharmacol.* 2006;62(5):552-559. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17061962>.
4. Nellen JF, Damming M, Godfried MH, et al. Steady-state nevirapine plasma concentrations are influenced by pregnancy. *HIV Med.* 2008;9(4):234-238. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18366447>.
5. Olagunju A, Bolaji O, Neary M, Back D, Khoo S, Owen A. Pregnancy affects nevirapine pharmacokinetics: evidence from a CYP2B6 genotype-guided observational study. *Pharmacogenet Genomics.* 2016;26(8):381-389. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27195527>.
6. Else LJ, Taylor S, Back DJ, Khoo SH. Pharmacokinetics of antiretroviral drugs in anatomical sanctuary sites: the fetal compartment (placenta and amniotic fluid). *Antivir Ther.* 2011;16(8):1139-1147. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22155898>.
7. Benaboud S, Ekouevi DK, Urien S, et al. Population pharmacokinetics of nevirapine in HIV-1-infected pregnant women and their neonates. *Antimicrob Agents Chemother.* 2011;55(1):331-337. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20956588>.
8. Palombi L, Pirillo MF, Andreotti M, et al. Antiretroviral prophylaxis for breastfeeding transmission in Malawi: drug

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- concentrations, virological efficacy and safety. *Antivir Ther.* 2012;17(8):1511-1519. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22910456>.
9. Shapiro RL, Rossi S, Ogwu A, et al. Therapeutic levels of lopinavir in late pregnancy and abacavir passage into breast milk in the Mma Bana Study, Botswana. *Antivir Ther.* 2013;18(4):585-590. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23183881>.
 10. Mirochnick M, Thomas T, Capparelli E, et al. Antiretroviral concentrations in breast-feeding infants of mothers receiving highly active antiretroviral therapy. *Antimicrob Agents Chemother.* 2009;53(3):1170-1176. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19114673>.
 11. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 July 2018. Wilmington, NC: Registry Coordinating Center. 2018. Available at: <http://www.apregistry.com/>.
 12. 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>.
 13. Patel SM, Johnson S, Belknap SM, Chan J, Sha BE, Bennett C. Serious adverse cutaneous and hepatic toxicities associated with nevirapine use by non-HIV-infected individuals. *J Acquir Immune Defic Syndr.* 2004;35(2):120-125. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14722442>.
 14. Stern JO, Robinson PA, Love J, Lanes S, Imperiale MS, Mayers DL. A comprehensive hepatic safety analysis of nevirapine in different populations of HIV infected patients. *J Acquir Immune Defic Syndr.* 2003;34 Suppl 1:S21-33. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14562855>.
 15. Mazhude C, Jones S, Murad S, Taylor C, Easterbrook P. Female sex but not ethnicity is a strong predictor of non-nucleoside reverse transcriptase inhibitor-induced rash. *AIDS.* 2002;16(11):1566-1568. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12131201>.
 16. Bersoff-Matcha SJ, Miller WC, Aberg JA, et al. Sex differences in nevirapine rash. *Clin Infect Dis.* 2001;32(1):124-129. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11118391>.
 17. Knudtson E, Para M, Boswell H, Fan-Havard P. Drug rash with eosinophilia and systemic symptoms syndrome and renal toxicity with a nevirapine-containing regimen in a pregnant patient with human immunodeficiency virus. *Obstet Gynecol.* 2003;101(5 Pt 2):1094-1097. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12738113>.
 18. Peters PJ, Stringer J, McConnell MS, et al. Nevirapine-associated hepatotoxicity was not predicted by CD4 count \geq 250 cells/ μ L among women in Zambia, Thailand and Kenya. *HIV Med.* 2010;11(10):650-660. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20659176>.
 19. Dong BJ, Zheng Y, Hughes MD, et al. Nevirapine pharmacokinetics and risk of rash and hepatitis among HIV-infected sub-Saharan African women. *AIDS.* 2012;26(7):833-841. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22301417>.
 20. Yuan J, Guo S, Hall D, et al. Toxicogenomics of nevirapine-associated cutaneous and hepatic adverse events among populations of African, Asian, and European descent. *AIDS.* 2011;25(10):1271-1280. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21505298>.
 21. Carr DF, Chaponda M, Jorgensen AL, et al. Association of human leukocyte antigen alleles and nevirapine hypersensitivity in a malawian HIV-infected population. *Clin Infect Dis.* 2013;56(9):1330-1339. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23362284>.
 22. Ciccacci C, Rufini S, Mancinelli S, et al. A pharmacogenetics study in Mozambican patients treated with nevirapine: full resequencing of TRAF3IP2 gene shows a novel association with SJS/TEN susceptibility. *Int J Mol Sci.* 2015;16(3):5830-5838. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25775161>.
 23. Carr DF, Chaponda M, Cornejo Castro EM, et al. CYP2B6 c.983T>C polymorphism is associated with nevirapine hypersensitivity in Malawian and Ugandan HIV populations. *J Antimicrob Chemother.* 2014;69(12):3329-3334. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25147095>.
 24. Lyons F, Hopkins S, Kelleher B, et al. Maternal hepatotoxicity with nevirapine as part of combination antiretroviral therapy in pregnancy. *HIV Med.* 2006;7(4):255-260. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16630038>.
 25. Ford N, Calmy A, Andrieux-Meyer I, Hargreaves S, Mills EJ, Shubber Z. Adverse events associated with nevirapine use in pregnancy: a systematic review and meta-analysis. *AIDS.* 2013. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23299174>.
 26. Ouyang DW, Brogly SB, Lu M, et al. Lack of increased hepatotoxicity in HIV-infected pregnant women receiving nevirapine compared with other antiretrovirals. *AIDS.* 2010;24(1):109-114. Available at: <http://www.ncbi.nlm.nih.gov/>

pubmed/19926957.

27. Ouyang DW, Shapiro DE, Lu M, et al. Increased risk of hepatotoxicity in HIV-infected pregnant women receiving antiretroviral therapy independent of nevirapine exposure. *AIDS*. 2009;23(18):2425-2430. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19617813>.
28. Huntington S, Thorne C, Anderson J, et al. Does pregnancy increase the risk of ART-induced hepatotoxicity among HIV-positive women? *J Int AIDS Soc*. 2014;17(4 Suppl 3):19486. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25393995>.
29. Bera E, Mia R. Safety of nevirapine in HIV-infected pregnant women initiating antiretroviral therapy at higher CD4 counts: a systematic review and meta-analysis. *S Afr Med J*. 2012;102(11 Pt 1):855-859. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23116743>.
30. Dube N, Adewusi E, Summers R. Risk of nevirapine-associated Stevens-Johnson syndrome among HIV-infected pregnant women: the Medunsa National Pharmacovigilance Centre, 2007 - 2012. *S Afr Med J*. 2013;103(5):322-325. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23971123>.
31. Zash R, Williams P, Jacobson D, et al. Increased risk of hypertension in pregnancy among women on nevirapine-based regimens. Poster 803. Presented at: Conference on Retroviruses and Opportunistic Infections. 2018. Boston, MA.
32. Kontorinis N, Dieterich DT. Toxicity of non-nucleoside analogue reverse transcriptase inhibitors. *Semin Liver Dis*. 2003;23(2):173-182. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12800070>.
33. Chappell CA, Lamorde M, Nakalema S, et al. Efavirenz decreases etonogestrel exposure: a pharmacokinetic evaluation of implantable contraception with antiretroviral therapy. *AIDS*. 2017;31(14):1965-1972. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28692531>.