

## Stopping Antiretroviral Drugs during Pregnancy (Last updated December 24, 2019; last reviewed December 24, 2019)

### Panel's Recommendations

- If an antiretroviral (ARV) drug regimen must be stopped during pregnancy (e.g., for severe toxicity), all ARV drugs should be stopped simultaneously, and a complete, effective antiretroviral therapy regimen should be reinitiated as soon as possible (AIII).

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Temporary discontinuation of antiretroviral (ARV) drug regimens during pregnancy may be indicated in some situations, including cases of serious drug-related toxicity, pregnancy-induced hyperemesis that is unresponsive to antiemetics, or acute illnesses or planned surgeries that prevent a patient from taking oral medications. Other reasons for discontinuing ARV drug regimens during pregnancy include a lack of available medication or patient request. The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission strongly recommends against discontinuing antiretroviral therapy (ART). **If a woman wants to discontinue ART during pregnancy or after delivery, it is strongly recommended that her clinician consult an HIV specialist for guidance (see Discontinuation or Interruption of Antiretroviral Therapy in the Adult and Adolescent Antiretroviral Guidelines).** If an ARV drug regimen must be stopped for any reason, all ARV drugs should be stopped simultaneously. ART should be reinitiated as soon as possible, whether the patient restarts the same regimen or initiates a new regimen.

Discontinuation of therapy could lead to an increase in viral load, with possible disease progression and decline in immune status. There may also be adverse consequences for the fetus, including an increased risk of *in utero* transmission of HIV. An analysis from a prospective cohort of 937 mother-child pairs found that interruption of ART during pregnancy, including interruption in the first and third trimesters, was independently associated with perinatal transmission of HIV. In the first trimester, the median gestational age at interruption was 6 weeks gestation and length of time without therapy was 8 weeks (interquartile range [IQR] 7–11 weeks); in the third trimester, the median gestational age at interruption was 32 weeks and length of time without therapy was 6 weeks (IQR 2–9 weeks). Although the perinatal transmission rate for the entire cohort was only 1.3%, transmission occurred in 4.9% of mother-child pairs (95% confidence interval [CI], 1.9% to 13.2%; adjusted odds ratio [aOR] 10.33;  $P = 0.005$ ) with first-trimester interruption and 18.2% of mother-child pairs (95% CI, 4.5% to 72.7%; aOR 46.96;  $P = 0.002$ ) with third-trimester interruption.<sup>1</sup>

Continuing all drugs during the intrapartum period is recommended. Women who are having elective cesarean delivery can take oral medications before the procedure and restart drugs following surgery. Because most drugs are given once or twice daily, it is likely that no doses would be missed or that the postpartum dose would be given a few hours late at most.

**Some ARV drugs, particularly non-nucleoside reverse transcriptase inhibitors, have longer serum half-lives than other ARV agents; if an ART regimen that contains these ARV drugs is stopped, the woman may have subtherapeutic blood levels of these agents. This exposes the patient to what is essentially monotherapy, which may lead to drug resistance.** For example, efavirenz can be detected in blood for longer than 3 weeks after discontinuation.<sup>2,3</sup> If an ARV drug that is known to have a long serum half-life must be stopped for more than a few days, clinicians should consider assessing the patient for rebound viremia and potential drug resistance and consider restarting an approved ART regimen when possible.<sup>4</sup> **If an ARV drug regimen must be stopped for any reason, all ARV drugs should be stopped simultaneously to minimize the disruption of viral suppression.**

In rare cases, a woman may not be able to meet the food requirements for certain ARV agents. In these instances, decisions about the ART administered during the antepartum or intrapartum period should be made on an individual basis and in consultation with an HIV treatment expert and a clinical pharmacologist who is

experienced with ARV medications.

## References

1. Galli L, Puliti D, Chiappini E, et al. Is the interruption of antiretroviral treatment during pregnancy an additional major risk factor for mother-to-child transmission of HIV type 1? *Clin Infect Dis*. 2009;48(9):1310-1317. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19309307>.
2. Sadiq ST, Fredericks S, Khoo SH, Rice P, Holt DW. Efavirenz detectable in plasma 8 weeks after stopping therapy and subsequent development of non-nucleoside reverse transcriptase inhibitor-associated resistance. *AIDS*. 2005;19(15):1716-1717. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16184054>.
3. Ribaud HJ, Haas DW, Tierney C, et al. Pharmacogenetics of plasma efavirenz exposure after treatment discontinuation: an adult AIDS clinical trials group study. *Clin Infect Dis*. 2006;42(3):401-407. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16392089>.
4. Geretti AM, Fox Z, Johnson JA, et al. Sensitive assessment of the virologic outcomes of stopping and restarting non-nucleoside reverse transcriptase inhibitor-based antiretroviral therapy. *PLoS One*. 2013;8(7):e69266. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23874928>.