
# Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection



Downloaded from http://aidsinfo.nih.gov/guidelines on 2/20/2013 EST.

## Table 17d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated November 1, 2012; last reviewed November 1, 2012) (page 1 of 2)

| Adverse Effects | Associated ARVs | Onset/Clinical Manifestations | Estimated Frequency | Risk Factors | Prevention / Monitoring | Management |
|---|---|---|---|---|---|---|
| Anemia[a] | Principally ZDV | Onset:<br>Variable, weeks to months<br><br>Presentation:<br>Most commonly asymptomatic or mild fatigue, pallor, tachypnea; rarely, congestive heart failure | HIV-exposed newborns:<br>Severe anemia uncommon, but may be seen coincident with physiologic Hgb nadir<br><br>HIV-infected children on ARVs:<br>2–3 times more common with ZDV-containing regimens; less frequent with currently recommended dosing of ZDV | HIV-exposed newborns:<br>Premature birth<br><br>*In utero* exposure to ARVs<br><br>Advanced maternal HIV<br><br>Neonatal blood loss<br><br>Concurrent ZDV + 3TC neonatal prophylaxis<br><br>HIV-infected children on ARVs:<br>Underlying hemoglobinopathy (sickle cell disease, G6PD deficiency)<br><br>Myelosuppressive drugs (e.g., TMP-SMX, rifabutin)<br><br>Iron deficiency<br><br>Advanced or poorly controlled HIV disease | HIV-exposed newborns:<br>Monitor CBC at birth.<br><br>Consider repeat CBC at 4 weeks for neonates who are at higher risk (such as those born prematurely or known to have low birth Hgb).<br><br>HIV-infected children on ARVs:<br>Avoid ZDV in children with moderate to severe anemia when alternative agents are available.<br><br>Monitor CBC 3–4 times per year as part of routine care. | HIV-exposed newborns:<br>Rarely require intervention unless Hgb is <7.0 g/dL or anemia is associated with symptoms.<br><br>Consider discontinuing ZDV if 4 weeks or more of 6-week ZDV prophylaxis regimen are already completed (see Perinatal Guidelines[b]).<br><br>HIV-infected children on ARVs:<br>Discontinue non-ARV marrow-toxic drugs, if feasible.<br><br>Treat coexisting iron deficiency, OIs, malignancies.<br><br>For persistent severe anemia thought to be associated with ARVs, change to a non-ZDV-containing regimen; consider a trial of erythropoietin. |

## Table 17d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated November 1, 2012; last reviewed November 1, 2012) (page 2 of 2)

| Adverse Effects | Associated ARVs | Onset/Clinical Manifestations | Estimated Frequency | Risk Factors | Prevention / Monitoring | Management |
|---|---|---|---|---|---|---|
| Neutropenia[a] | Principally ZDV | Onset: Variable<br><br>Presentation: Most commonly asymptomatic | HIV-exposed newborns: Rare<br><br>HIV-infected children on ARVs: 9.9%–26.8% of children on ARVs, depending upon the ARV regimen<br><br>Highest rates with ZDV-containing regimens | HIV-exposed newborns: *In utero* exposure to ARVs<br><br>Concurrent ZDV + 3TC neonatal prophylaxis<br><br>HIV-infected children on ARVs: Advanced or poorly controlled HIV infection<br><br>Myelosuppressive drugs (such as TMP-SMX, ganciclovir, hydroxyurea, rifabutin) | HIV-infected children on ARVs: Monitor CBC 3–4 times per year as part of routine care. | HIV-exposed newborns: No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC <500 cells/μL, or discontinue ARV prophylaxis entirely if ≥4 weeks of 6-week ZDV prophylaxis have been completed (see Perinatal Guidelines[b]).<br><br>HIV-infected children on ARVs: Discontinue non-ARV marrow-toxic drugs if feasible.<br><br>Treat coexisting OIs, malignancies.<br><br>For persistent severe neutropenia thought to be associated with ARVs, change to a non-ZDV-containing regimen; consider a trial of G-CSF. |

[a] HIV infection itself, OIs, and medications used to prevent OIs, such as TMP-SMX, may all contribute to anemia, neutropenia, and thrombocytopenia.

[b] *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*

**Key to Acronyms:** 3TC = lamivudine, ANC = absolute neutrophil count, ARV = antiretroviral, CBC = complete blood count, G6PD = glucose-6-phosphate dehydrogenase, G-CSF = granulocyte colony-stimulating factor, Hgb = hemoglobin, NRTI = nucleoside reverse transcriptase inhibitor, OIs = opportunistic infections, TMP-SMX = trimethoprim-sulfamethoxazole, ZDV = zidovudine

## References


1. Englund JA, Baker CJ, Raskino C, et al. Zidovudine, didanosine, or both as the initial treatment for symptomatic HIV-infected children. AIDS Clinical Trials Group (ACTG) Study 152 Team. *N Engl J Med*. Jun 12 1997;336(24):1704-1712. Available at http://www.ncbi.nlm.nih.gov/pubmed/9182213.
2. Starr SE, Fletcher CV, Spector SA, et al. Combination therapy with efavirenz, nelfinavir, and nucleoside reverse-transcriptase inhibitors in children infected with human immunodeficiency virus type 1. Pediatric AIDS Clinical Trials Group 382 Team. *N Engl J Med*. Dec 16 1999;341(25):1874-1881. Available at http://www.ncbi.nlm.nih.gov/pubmed/10601506.
3. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med*. Nov 3 1994;331(18):1173-1180. Available at http://www.ncbi.nlm.nih.gov/pubmed/7935654.
4. Krogstad P, Lee S, Johnson G, et al. Nucleoside-analogue reverse-transcriptase inhibitors plus nevirapine, nelfinavir, or ritonavir for pretreated children infected with human immunodeficiency virus type 1. *Clin Infect Dis*. Apr 1 2002;34(7):991-1001. Available at http://www.ncbi.nlm.nih.gov/pubmed/11880966.
5. McKinney RE, Jr., Johnson GM, Stanley K, et al. A randomized study of combined zidovudine-lamivudine versus didanosine monotherapy in children with symptomatic therapy-naive HIV-1 infection. The Pediatric AIDS Clinical Trials Group Protocol 300 Study Team. *J Pediatr*. Oct 1998;133(4):500-508. Available at http://www.ncbi.nlm.nih.gov/pubmed/9787687.
6. Najean Y, Rain JD. The mechanism of thrombocytopenia in patients with HIV infection. *The Journal of laboratory and clinical medicine*. Mar 1994;123(3):415-420. Available at http://www.ncbi.nlm.nih.gov/pubmed/8133154.
7. Caselli D, Maccabruni A, Zuccotti GV, et al. Recombinant erythropoietin for treatment of anaemia in HIV-infected children. *AIDS*. Jul 1996;10(8):929-931. Available at http://www.ncbi.nlm.nih.gov/pubmed/8828757.
8. Allen UD, Kirby MA, Goeree R. Cost-effectiveness of recombinant human erythropoietin versus transfusions in the treatment of zidovudine-related anemia in HIV-infected children. *Pediatric AIDS and HIV infection*. Feb 1997;8(1):4-11. Available at http://www.ncbi.nlm.nih.gov/pubmed/11361510.
9. Mueller BU, Jacobsen F, Butler KM, Husson RN, Lewis LL, Pizzo PA. Combination treatment with azidothymidine and granulocyte colony-stimulating factor in children with human immunodeficiency virus infection. *J Pediatr*. Nov 1992;121(5 Pt 1):797-802. Available at http://www.ncbi.nlm.nih.gov/pubmed/1279153.
10. Bussel JB, Graziano JN, Kimberly RP, Pahwa S, Aledort LM. Intravenous anti-D treatment of immune thrombocytopenic purpura: analysis of efficacy, toxicity, and mechanism of effect. *Blood*. May 1 1991;77(9):1884-1893. Available at http://www.ncbi.nlm.nih.gov/pubmed/1850307.
11. Scaradavou A, Woo B, Woloski BM, et al. Intravenous anti-D treatment of immune thrombocytopenic purpura: experience in 272 patients. *Blood*. Apr 15 1997;89(8):2689-2700. Available at http://www.ncbi.nlm.nih.gov/pubmed/9108386.
12. Lahoz R, Noguera A, Rovira N, et al. Antiretroviral-related hematologic short-term toxicity in healthy infants: implications of the new neonatal 4-week zidovudine regimen. *Pediatr Infect Dis J*. Apr 2010;29(4):376-379. Available at http://www.ncbi.nlm.nih.gov/pubmed/19949355.
13. Dryden-Peterson S, Shapiro RL, Hughes MD, et al. Increased risk of severe infant anemia after exposure to maternal HAART, Botswana. *J Acquir Immune Defic Syndr*. Apr 15 2011;56(5):428-436. Available at http://www.ncbi.nlm.nih.gov/pubmed/21266910.
14. Mocroft A, Lifson AR, Touloumi G, et al. Haemoglobin and anaemia in the SMART study. *Antivir Ther*. 2011;16(3):329-337. Available at http://www.ncbi.nlm.nih.gov/pubmed/21555815.