



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

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 7/11/2017

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

# Zidovudine (ZDV, AZT, Retrovir) (Last updated April 27, 2017; last reviewed April 27, 2017)

For additional information see Drugs@FDA: <http://www.accessdata.fda.gov/scripts/cder/daf/>

## Formulations

**Capsules:** 100 mg

**Tablets:** 300 mg

**Syrup:** 10 mg/mL

**Concentrate for Injection or Intravenous (IV) Infusion:** 10 mg/mL

**Generic Formulations:** Zidovudine capsules, tablets, syrup, and injection are approved by the Food and Drug Administration for manufacture and distribution in the United States.

### Fixed-Dose Combination Tablets:

- [Combivir and Generic] Lamivudine 150 mg plus zidovudine 300 mg
- [Trizivir] Abacavir 300 mg plus lamivudine 150 mg plus zidovudine 300 mg

## Dosing Recommendations

Recommended Neonatal Dose for Treatment of HIV <sup>a</sup>									
<b>Weeks' Gestation at Birth</b>	<b>Zidovudine Oral Dosing:</b> <ul style="list-style-type: none"><li>• Twice-Daily Dosing</li></ul> <p><b>Note:</b> For infants unable to tolerate oral agents, the IV dose should be 75% of the oral dose while maintaining the same dosing interval.</p>								
<b>≥35 Weeks' Gestation at Birth</b>	<p><b>Birth to Age 4 Weeks:</b></p> <ul style="list-style-type: none"><li>• 4 mg/kg orally twice daily or alternative simplified weight band dosing</li></ul> <p><b>Simplified Weight Band Dosing for Infants Aged ≥35 Weeks:</b></p> <p><b>Note:</b> Provides approximately 4 mg/kg orally twice daily from birth to 4 weeks of age</p> <table><tr><th>Weight Band (kg)</th><th>Volume (mL) ZDV 10 mg/mL Oral Syrup Twice Daily</th></tr><tr><td>2 to &lt;3 kg</td><td>1 mL</td></tr><tr><td>3 to &lt;4 kg</td><td>1.5 mL</td></tr><tr><td>4 to &lt;5 kg</td><td>2 mL</td></tr></table> <p><b>Aged &gt;4 Weeks:</b></p> <ul style="list-style-type: none"><li>• 12 mg/kg orally twice daily</li></ul>	Weight Band (kg)	Volume (mL) ZDV 10 mg/mL Oral Syrup Twice Daily	2 to <3 kg	1 mL	3 to <4 kg	1.5 mL	4 to <5 kg	2 mL
Weight Band (kg)	Volume (mL) ZDV 10 mg/mL Oral Syrup Twice Daily								
2 to <3 kg	1 mL								
3 to <4 kg	1.5 mL								
4 to <5 kg	2 mL								
<b>≥30 to &lt;35 Weeks' Gestation at Birth</b>	<p><b>Birth to Age 2 Weeks:</b></p> <ul style="list-style-type: none"><li>• 2 mg/kg orally twice daily</li></ul> <p><b>Aged 2 Weeks to 6 to 8 Weeks:</b></p> <ul style="list-style-type: none"><li>• 3 mg/kg orally twice daily</li></ul> <p><b>Aged &gt;6 to 8 Weeks:</b></p> <ul style="list-style-type: none"><li>• 12 mg/kg orally twice daily</li></ul>								

## Selected Adverse Events

- Bone marrow suppression: macrocytosis with or without anemia, neutropenia
- Nausea, vomiting, headache, insomnia, asthenia
- Lactic acidosis/severe hepatomegaly with hepatic steatosis
- Lipodystrophy and lipoatrophy
- Myopathy (associated with prolonged use) and myositis

## Special Instructions

- Give zidovudine without regard to food.
- If substantial granulocytopenia or anemia develops in patients receiving zidovudine, it may be necessary to discontinue therapy until bone marrow recovery is observed. In this setting, some patients may require erythropoietin or filgrastim injections or transfusions of red blood cells.

## Metabolism/Elimination

- Metabolized primarily in the liver to zidovudine glucuronide, which is renally excreted.
- Zidovudine is phosphorylated intracellularly to active zidovudine-triphosphate.
- Dosing in patients with renal impairment: Dosage adjustment is required in renal

Recommended Neonatal Dosing for Treatment of HIV <sup>a</sup>	
<30 Weeks' Gestation at Birth	<b>Birth to Age 4 Weeks:</b>
	• 2 mg/kg orally twice daily
	<b>Aged 4 Weeks to 8 to 10 Weeks:</b>
	• 3 mg/kg orally twice daily
	<b>Aged &gt;8 to 10 Weeks:</b>
	• 12 mg/kg orally twice daily

<sup>a</sup> For prevention of perinatal transmission see [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](#).

### Infant/Child Dose (Age ≥35 Weeks Post-Conception and ≥4 Weeks Post-Delivery with Body Weight ≥4 kg):

#### Weight-Based Dosing

Body Weight	Twice-Daily Dosing
4 kg to <9 kg	12 mg/kg
9 kg to <30 kg	9 mg/kg
≥30 kg	300 mg

#### Alternative Body Surface Area Dosing:

- Oral: 180–240 mg/m<sup>2</sup> body surface area every 12 hours

#### Adolescent (Aged ≥18 Years) and Adult Dose:

- 300 mg twice daily

#### [Combivir and Generic] Lamivudine plus Zidovudine

Adolescent (Weight ≥30 kg) and Adult Dose:

- 1 tablet twice daily

#### [Trizivir] Abacavir plus Lamivudine plus Zidovudine

Adolescent (Weight ≥40 kg) and Adult Dose:

- 1 tablet twice daily

insufficiency.

- Dosing in patients with hepatic impairment: Decreased dosing may be required in patients with hepatic impairment.
- Do not use fixed-dose combination products (e.g., Combivir, Trizivir) in patients with creatinine clearance <50 mL/min, on dialysis, or who have impaired hepatic function.

### Drug Interactions (see also the [Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents](#))

- *Other nucleoside reverse transcriptase inhibitors (NRTIs):* Zidovudine should not be administered in combination with stavudine because of *in vitro* virologic antagonism.
- *Bone marrow suppressive/cytotoxic agents including ganciclovir, valganciclovir, interferon alfa, and ribavirin:* These agents may increase the hematologic toxicity of zidovudine.
- *Nucleoside analogues affecting DNA replication:* Nucleoside analogues such as ribavirin antagonize *in vitro* antiviral activity of zidovudine.
- *Doxorubicin:* Simultaneous use of doxorubicin and zidovudine should be avoided. Doxorubicin may inhibit the phosphorylation of zidovudine to its active form.

## Major Toxicities

- *More common:* Hematologic toxicity, including granulocytopenia and anemia, particularly in patients with advanced HIV-1 disease. Headache, malaise, nausea, vomiting, and anorexia. Incidence of neutropenia may be increased in infants receiving lamivudine.<sup>1</sup>
- *Less common (more severe):* Myopathy (associated with prolonged use), myositis, and liver toxicity. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported. Fat maldistribution.
- *Rare:* Increased risk of hypospadias after first-trimester exposure to zidovudine observed in one cohort study.<sup>2</sup> Possible increased risk of cardiomyopathy.<sup>3</sup> Possible association between first-trimester exposure to zidovudine and congenital heart defects (see [Teratogenicity](#) in the [Perinatal Guidelines](#)).<sup>4-6</sup>

## Resistance

The International Antiviral Society-USA (IAS-USA) maintains a list of updated resistance mutations (see [http://iasusa.org/sites/default/files/tam/october\\_november\\_2015.pdf#page=10](http://iasusa.org/sites/default/files/tam/october_november_2015.pdf#page=10)) and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation (see <http://hivdb.stanford.edu/pages/GRIP/zidovudine.html>).

## Pediatric Use

### Approval

Zidovudine is frequently included as a component of the NRTI backbone for antiretroviral therapy (ART) and has been studied in children in combination with abacavir, didanosine, or lamivudine.<sup>7-23</sup> Pediatric experience with zidovudine both for treatment of HIV and for prevention of perinatal transmission is extensive.

### Efficacy in Clinical Trials

#### Zidovudine in Combination with Lamivudine

- Zidovudine with lamivudine has been extensively studied in children and has been a part of ART regimens in many trials.
- Zidovudine combined with lamivudine was compared to abacavir plus lamivudine and stavudine plus lamivudine in children aged <5 years in the CHAPAS-3 study. All regimens also contained either nevirapine or efavirenz. All NRTIs had low toxicity and good clinical, immunologic, and virologic responses.<sup>24</sup>

#### Zidovudine in Combination with Abacavir or Didanosine

- In a large pediatric study, the combination of zidovudine and didanosine had the lowest rate of toxicities.<sup>25</sup>
- Zidovudine/abacavir and zidovudine/lamivudine had lower rates of viral suppression and more toxicity leading to drug modification than did abacavir/lamivudine in a European pediatric study.<sup>26,27</sup>

### Special Issues in Neonates

Perinatal trial PACTG 076 established that zidovudine prophylaxis given during pregnancy, labor, and delivery, and to the newborn reduced risk of perinatal transmission of HIV by nearly 70%<sup>28</sup> (see the [Perinatal Guidelines](#) for further discussion on the use of zidovudine for the prevention of perinatal transmission of HIV). Zidovudine 4 mg/kg body weight every 12 hours (prophylactic dose) is recommended for neonates/infants  $\geq 35$  weeks' gestation for prevention of transmission (see the [Perinatal Guidelines](#)). Infants who are HIV-exposed but uninfected should be continued on the prophylactic dose for 4 to 6 weeks **depending on assessment of risk for perinatal transmission and gestational age at time of delivery** (see [Perinatal Guidelines](#)).

For full-term neonates who are diagnosed with HIV, the zidovudine dose should be increased at age 4 weeks to the continuation dose (**see dosing table**). The activity of the enzymes responsible for glucuronidation is

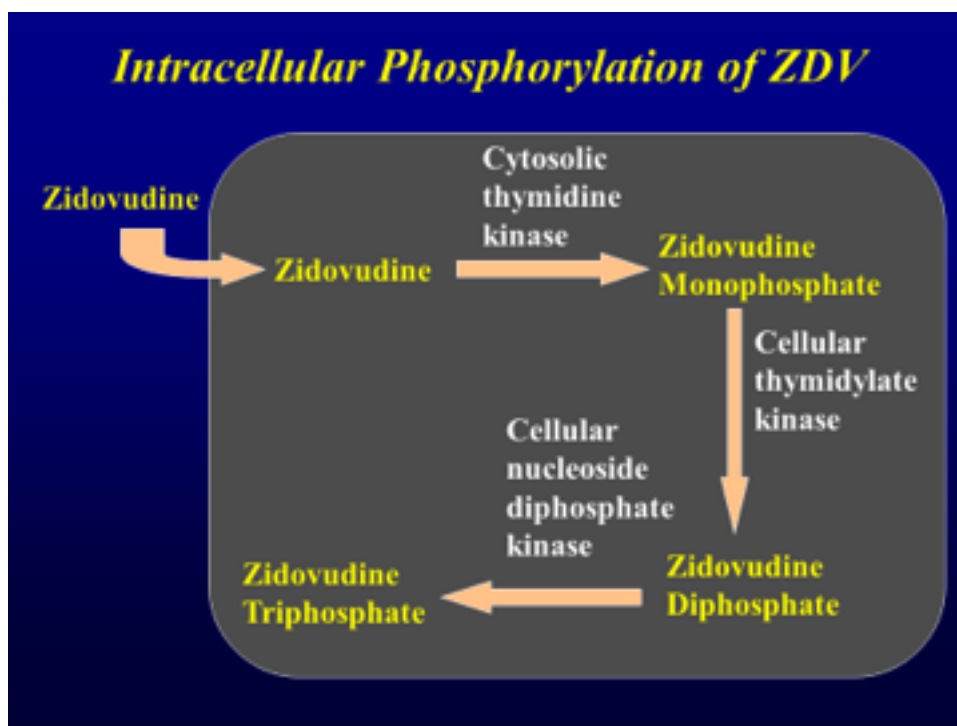
low at birth and increases dramatically over the first 4 to 6 weeks of life in full-term neonates.

For premature infants who are diagnosed with HIV infection, the time to change the dose to continuation dose varies with post-gestational age and clinical status of the neonate. Based on modeling and pharmacokinetics (PK) of zidovudine in premature infants, for infants born at  $\geq 30$  to  $< 35$  weeks change to 12 mg/kg/dose at post-gestational age 6 to 8 weeks and for infants  $< 30$  weeks, change to 12 mg/kg at post-gestational age 8 to 10 weeks.<sup>29</sup> Careful clinical assessment of the infant, evaluation of hepatic and renal function, and review of concomitant medications should be performed prior to increasing zidovudine dose to that recommended for full-term infants.

### ***Pharmacokinetics***

Overall, zidovudine PK in pediatric patients aged  $> 3$  months are similar to those in adults. Zidovudine undergoes intracellular metabolism to its active form, zidovudine triphosphate. Although the mean half-life of intracellular zidovudine triphosphate (9.1 hours) is considerably longer than that of unmetabolized zidovudine in plasma (1.5 hours), once-daily zidovudine dosing is not recommended because of low intracellular zidovudine triphosphate concentrations seen with 600-mg, once-daily dosing in adolescents.<sup>30</sup> PK studies such as PACTG 331 demonstrate that dose adjustments are necessary for premature infants because they have reduced clearance of zidovudine compared with term newborns of similar postnatal age.<sup>8</sup> Zidovudine has good central nervous system (CNS) penetration (cerebrospinal fluid-to-plasma concentration ratio = 0.68) and has been used in children with HIV-related CNS disease.<sup>19</sup>

**Figure A: Intracellular Phosphorylation of ZDV**



Source: Mirochnick M. Antiretroviral pharmacology in pregnant women and their newborns. Presented at: Advances in Pediatric AIDS. 1999. Montreal, CA.

The rate-limiting step in phosphorylation is the thymidylate kinase. Increasing doses of zidovudine will lead to increased zidovudine plasma concentrations and increased intracellular concentrations of zidovudine monophosphate but not zidovudine diphosphate or zidovudine triphosphate. In 31 infants receiving zidovudine for prevention of perinatal transmission, intracellular zidovudine metabolites were measured after delivery. Plasma zidovudine and intracellular zidovudine monophosphate decreased by roughly 50% when compared on post-delivery day 1 to day 28, whereas the zidovudine diphosphate and zidovudine triphosphate remained

low throughout the sampling period.<sup>31</sup> Based on the poor correlation between zidovudine dose and intracellular zidovudine triphosphate concentrations, a simplified dosing approach for infants  $\geq 35$  weeks gestation receiving approximately 4 mg/kg twice daily oral dosing for the first 4 weeks of life is proposed (see dosing table). These volumes provide approximately 4 mg/kg per dose using the 10 mg/mL oral syrup. This approach should simplify the minor dose adjustments that are commonly made based on changes in infant weight during zidovudine use in the first 4 weeks of life. These changes in weight and small differences in ZDV dose will have minor effects on the intracellular concentrations of zidovudine triphosphate. This approach should make it easier for caregivers to administer zidovudine oral syrup to their infants.

### Toxicity

Several studies suggest that the adverse hematologic effects of zidovudine may be concentration-dependent, with a higher risk of anemia and neutropenia in patients with higher mean area under the curve.<sup>7,8,32</sup>

Incidence of hematological toxicity was compared in the ARROW study of Ugandan/Zimbabwean treatment-naïve children randomized to zidovudine- versus abacavir-containing regimens. The incidence of severe anemia was similar regardless of zidovudine use and suggests that advanced HIV disease contributed to low hemoglobin values. Zidovudine use was associated with severe neutropenia in a small number of children.<sup>33</sup>

Zidovudine is associated with greater mitochondrial toxicity when compared to abacavir and tenofovir disoproxil fumarate but less than stavudine.<sup>34,35</sup>

While the incidence of cardiomyopathy associated with perinatal HIV infection has decreased dramatically since use of ART became routine, a regimen containing zidovudine may increase the risk.<sup>3</sup> Recent analysis of data from a US-based, multicenter prospective cohort study (PACTG 219/219C) found that ongoing zidovudine exposure was independently associated with a higher rate of cardiomyopathy.<sup>3</sup>

### References

1. Nielsen-Saines K, Watts DH, Veloso VG, et al. Three postpartum antiretroviral regimens to prevent intrapartum HIV infection. *N Engl J Med*. 2012;366(25):2368-2379. Available at <http://www.ncbi.nlm.nih.gov/pubmed/22716975>.
2. Watts DH, Li D, Handelsman E, et al. Assessment of birth defects according to maternal therapy among infants in the Women and Infants Transmission Study. *J Acquir Immune Defic Syndr*. 2007;44(3):299-305. Available at <http://www.ncbi.nlm.nih.gov/pubmed/17159659>.
3. Patel K, Van Dyke RB, Mittleman MA, et al. The impact of HAART on cardiomyopathy among children and adolescents perinatally infected with HIV-1. *AIDS*. 2012;26(16):2027-2037. Available at <http://www.ncbi.nlm.nih.gov/pubmed/22781228>.
4. 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>.
5. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. 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. 2016. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf>.
6. Sibiude J, Le Chenadec J, Bonnet D, et al. In utero exposure to zidovudine and heart anomalies in the ANRS French perinatal cohort and the nested PRIMEVA randomized trial. *Clin Infect Dis*. 2015;61(2):270-280. Available at <http://www.ncbi.nlm.nih.gov/pubmed/25838291>.
7. Balis FM, Pizzo PA, Murphy RF, et al. The pharmacokinetics of zidovudine administered by continuous infusion in children. *Ann Intern Med*. 1989;110(4):279-285. Available at <http://www.ncbi.nlm.nih.gov/pubmed/2643914>.
8. Capparelli EV, Mirochnick M, Dankner WM, et al. Pharmacokinetics and tolerance of zidovudine in preterm infants. *J Pediatr*. 2003;142(1):47-52. Available at <http://www.ncbi.nlm.nih.gov/pubmed/12520254>.
9. Chadwick EG, Rodman JH, Britto P, et al. Ritonavir-based highly active antiretroviral therapy in human



immunodeficiency virus type 1-infected infants younger than 24 months of age. *Pediatr Infect Dis J*. 2005;24(9):793-800. Available at <http://www.ncbi.nlm.nih.gov/pubmed/16148846>.

10. 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*. 1997;336(24):1704-1712. Available at <http://www.ncbi.nlm.nih.gov/pubmed/9182213>.
11. Jankelevich S, Mueller BU, Mackall CL, et al. Long-term virologic and immunologic responses in human immunodeficiency virus type 1-infected children treated with indinavir, zidovudine, and lamivudine. *J Infect Dis*. 2001;183(7):1116-1120. Available at <http://www.ncbi.nlm.nih.gov/pubmed/11237839>.
12. King JR, Kimberlin DW, Aldrovandi GM, Acosta EP. Antiretroviral pharmacokinetics in the paediatric population: a review. *Clinical Pharmacokinetics*. 2002;41(14):1115-1133. Available at <http://www.ncbi.nlm.nih.gov/pubmed/12405863>.
13. Luzuriaga K, Bryson Y, Krogstad P, et al. Combination treatment with zidovudine, didanosine, and nevirapine in infants with human immunodeficiency virus type 1 infection. *N Engl J Med*. 1997;336(19):1343-1349. Available at <http://www.ncbi.nlm.nih.gov/pubmed/9134874>.
14. McKinney RE, Jr., Maha MA, Connor EM, et al. A multicenter trial of oral zidovudine in children with advanced human immunodeficiency virus disease. The Protocol 043 Study Group. *N Engl J Med*. 1991;324(15):1018-1025. Available at <http://www.ncbi.nlm.nih.gov/pubmed/1672443>.
15. McKinney RE, Jr., Johnson GM, Stanley K, et al. A randomized study of combined zidovudine-lamivudine versus didanosine monotherapy in children with symptomatic therapy-naïve HIV-1 infection. The Pediatric AIDS Clinical Trials Group Protocol 300 Study Team. *J Pediatr*. 1998;133(4):500-508. Available at <http://www.ncbi.nlm.nih.gov/pubmed/9787687>.
16. Mueller BU, Nelson RP, Jr., Sleasman J, et al. A phase I/II study of the protease inhibitor ritonavir in children with human immunodeficiency virus infection. *Pediatrics*. 1998;101(3 Pt 1):335-343. Available at <http://www.ncbi.nlm.nih.gov/pubmed/9480994>.
17. Mueller BU, Sleasman J, Nelson RP Jr, et al. A phase I/II study of the protease inhibitor indinavir in children with HIV infection. *Pediatrics*. 1998;102(1 Pt 1):101-109. Available at <http://www.ncbi.nlm.nih.gov/pubmed/9651421>.
18. Palacios GC, Palafox VL, Alvarez-Munoz MT, et al. Response to two consecutive protease inhibitor combination therapy regimens in a cohort of HIV-1-infected children. *Scand J Infect Dis*. 2002;34(1):41-44. Available at <http://www.ncbi.nlm.nih.gov/pubmed/11874163>.
19. Pizzo PA, Eddy J, Falloon J, et al. Effect of continuous intravenous infusion of zidovudine (AZT) in children with symptomatic HIV infection. *N Engl J Med*. 1988;319(14):889-896. Available at <http://www.ncbi.nlm.nih.gov/pubmed/3166511>.
20. Saez-Llorens X, Nelson RP, Jr., Emmanuel P, et al. A randomized, double-blind study of triple nucleoside therapy of abacavir, lamivudine, and zidovudine versus lamivudine and zidovudine in previously treated human immunodeficiency virus type 1-infected children. The CNAA3006 Study Team. *Pediatrics*. 2001;107(1):E4. Available at <http://www.ncbi.nlm.nih.gov/pubmed/11134468>.
21. van Rossum AM, Geelen SP, Hartwig NG, et al. Results of 2 years of treatment with protease-inhibitor--containing antiretroviral therapy in dutch children infected with human immunodeficiency virus type 1. *Clin Infect Dis*. 2002;34(7):1008-1016. Available at <http://www.ncbi.nlm.nih.gov/pubmed/11880968>.
22. Bergshoeff AS, Fraaij PL, Verweij C, et al. Plasma levels of zidovudine twice daily compared with three times daily in six HIV-1-infected children. *J Antimicrob Chemother*. 2004;54(6):1152-1154. Available at <http://www.ncbi.nlm.nih.gov/pubmed/15537694>.
23. Nachman SA, Stanley K, Yogev R, et al. Nucleoside analogs plus ritonavir in stable antiretroviral therapy-experienced HIV-infected children: a randomized controlled trial. Pediatric AIDS Clinical Trials Group 338 Study Team. *JAMA*. 2000;283(4):492-498. Available at <http://www.ncbi.nlm.nih.gov/pubmed/10659875>.
24. Mulenga V, Musiime V, Kekitiinwa A, et al. Abacavir, zidovudine, or stavudine as paediatric tablets for African HIV-infected children (CHAPAS-3): an open-label, parallel-group, randomised controlled trial. *Lancet Infect Dis*. 2016;16(2):169-179. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26481928>.

25. Van Dyke RB, Wang L, Williams PL, Pediatric ACTGCT. Toxicities associated with dual nucleoside reverse-transcriptase inhibitor regimens in HIV-infected children. *J Infect Dis*. 2008;198(11):1599-1608. Available at <http://www.ncbi.nlm.nih.gov/pubmed/19000014>.
26. Green H, Gibb DM, Walker AS, et al. Lamivudine/abacavir maintains virological superiority over zidovudine/lamivudine and zidovudine/abacavir beyond 5 years in children. *AIDS*. 2007;21(8):947-955. Available at <http://www.ncbi.nlm.nih.gov/pubmed/17457088>.
27. Paediatric European Network for Treatment of AIDS (PENTA). Comparison of dual nucleoside-analogue reverse-transcriptase inhibitor regimens with and without nelfinavir in children with HIV-1 who have not previously been treated: the PENTA 5 randomised trial. *Lancet*. 2002;359(9308):733-740. Available at [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=11888583&query\\_hl=42](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11888583&query_hl=42).
28. 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*. 1994;331(18):1173-1180. Available at <http://www.ncbi.nlm.nih.gov/pubmed/7935654>.
29. Capparelli EV, Englund JA, Connor JD, et al. Population pharmacokinetics and pharmacodynamics of zidovudine in HIV-infected infants and children. *J Clin Pharmacol*. 2003;43(2):133-140. Available at <http://www.ncbi.nlm.nih.gov/pubmed/12616665>.
30. Flynn PM, Rodman J, Lindsey JC, et al. Intracellular pharmacokinetics of once versus twice daily zidovudine and lamivudine in adolescents. *Antimicrob Agents Chemother*. 2007;51(10):3516-3522. Available at <http://www.ncbi.nlm.nih.gov/pubmed/17664328>.
31. Kinai E, Kato S, Hosokawa S, et al. High plasma concentrations of zidovudine (AZT) do not parallel intracellular concentrations of AZT-triphosphates in infants during prevention of mother-to-child HIV-1 transmission. *J Acquir Immune Defic Syndr*. 2016;72(3):246-253. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26859826>.
32. Fillekes Q, Kendall L, Kitaka S, et al. Pharmacokinetics of zidovudine dosed twice daily according to World Health Organization weight bands in Ugandan HIV-infected children. *Pediatr Infect Dis J*. 2014;33(5):495-498. Available at <http://www.ncbi.nlm.nih.gov/pubmed/24736440>.
33. Musiime V, Cook A, Nahirya Ntege P, et al. The effect of long-term zidovudine on hematological parameters in the ARROW randomized trial. Presented at: The 22nd Conference on Retroviruses and Opportunistic Infections. 2015. Seattle, WA.
34. Moyle GJ, Sabin CA, Cartledge J, et al. A randomized comparative trial of tenofovir DF or abacavir as replacement for a thymidine analogue in persons with lipoatrophy. *AIDS*. 2006;20(16):2043-2050. Available at <http://www.ncbi.nlm.nih.gov/pubmed/17053350>.
35. Carr A, Workman C, Smith DE, et al. Abacavir substitution for nucleoside analogs in patients with HIV lipoatrophy: a randomized trial. *JAMA*. 2002;288(2):207-215. Available at <http://www.ncbi.nlm.nih.gov/pubmed/12095385>.