

# Abacavir (ABC, Ziagen)

Updated: April 11, 2023

Reviewed: April 11, 2023

Formulations	
<p><b>Pediatric Oral Solution:</b> 20 mg/mL</p> <p><b>Tablet:</b> 300 mg (scored)</p> <p><b>Generic Formulations</b></p> <ul style="list-style-type: none"> <li>• 300-mg tablet</li> <li>• 20 mg/mL pediatric oral solution</li> </ul> <p><b>Fixed-Dose Combination Tablets</b></p> <ul style="list-style-type: none"> <li>• [Epzicom and generic] Abacavir 600 mg/lamivudine 300 mg</li> <li>• [Triumeq] Abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg</li> <li>• [Triumeq PD] Abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg</li> </ul> <p>When using fixed-dose combination (FDC) tablets, refer to other sections of <a href="#">Appendix A: Pediatric Antiretroviral Drug Information</a> for information about the individual components of the FDC. See also <a href="#">Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents</a>.</p> <p>For additional information, see <a href="#">Drugs@FDA</a> or <a href="#">DailyMed</a>.</p>	
Dosing Recommendations	Selected Adverse Events
<p><b>Neonate (Aged Birth Through &lt;1 Month) Dose</b></p> <p><i>Oral Solution</i></p> <ul style="list-style-type: none"> <li>• Abacavir (ABC) is not approved by the U.S. Food and Drug Administration (FDA) for use in neonates aged &lt;1 month.</li> <li>• The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) recommends ABC 2 mg/kg twice daily for full-term infants from birth through &lt;1 month of age. This recommendation is based on data from pharmacokinetic (PK) modeling of neonatal ABC dosing to target adult plasma ABC exposures, and observational data supporting safety of ABC in neonates. The World Health Organization (WHO) <a href="#">Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery, and Monitoring</a> Annex 1: Dosages for ARV Drugs provides weight-band dosing recommendations for full-term neonates based on the same data. See Approval, Pharmacokinetics in Neonates and Infants, and Safety in Neonates and Infants sections below.</li> </ul>	<ul style="list-style-type: none"> <li>• Hypersensitivity reactions (HSRs) can be fatal. HSRs usually occur during the first few weeks of starting therapy. Symptoms may include fever, rash, nausea, vomiting, malaise or fatigue, loss of appetite, and respiratory symptoms (e.g., cough, shortness of breath).</li> </ul>
	<p><b>Special Instructions</b></p> <ul style="list-style-type: none"> <li>• Test patients for the HLA-B*5701 allele before starting therapy to predict the risk of HSRs. Patients who test positive for the HLA-B*5701 allele should not be given ABC. Patients with no prior HLA-B*5701 testing who are tolerating ABC do not need to be tested.</li> <li>• Warn patients and caregivers about the risk of serious, potentially fatal HSRs. Occurrence of an HSR requires <b>immediate and permanent discontinuation of ABC. Do not rechallenge.</b></li> <li>• ABC can be given without food. The oral solution does not require refrigeration.</li> </ul>

<p><b>Infant (Aged ≥1 Month to &lt;3 Months) Dose</b></p> <p><i>Oral Solution</i></p> <ul style="list-style-type: none"><li>• ABC is not approved by the FDA for use in infants aged &lt;3 months.</li><li>• The Panel recommends ABC 4 mg/kg twice daily in full-term infants aged ≥1 month to &lt;3 months. This recommendation is based on modeling data of the ABC 4 mg/kg twice-daily dose using PK simulation for full-term infants aged ≥1 month to &lt;3 months. The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1106 study and two observational cohorts provide reassuring data on the safety of ABC in infants with HIV aged &lt;3 months. See Approval, Pharmacokinetics in Neonates and Infants, and Safety in Neonates and Infants sections below.</li></ul>	<ul style="list-style-type: none"><li>• For ABC/DTG/3TC dispersible tablets, fully disperse them in 20 mL of drinking water in the supplied cup and swirl the suspension so that no lumps remain. After full dispersion and within 30 minutes of mixing, administer the oral suspension. Rinse the dosing cup with a small amount of water and give this additional water to the child to ensure that the child takes the full dose and no medication remains in the dosing cup. ABC/DTG/3TC dispersible tablets should not be swallowed whole, chewed, cut, or crushed.</li><li>• Screen patients for hepatitis B virus (HBV) infection before using ABC FDC tablets that contain lamivudine (3TC). Severe acute exacerbation of HBV infection can occur when 3TC is discontinued (see <a href="#">Lamivudine</a>).</li></ul>															
<p><b>Infant and Child (Aged ≥3 Months) Dose</b></p> <p><i>Oral Solution</i></p> <ul style="list-style-type: none"><li>• ABC 8 mg/kg twice daily (maximum 300 mg per dose) or ABC 16 mg/kg once daily (maximum 600 mg per dose)</li><li>• In infants and young children who are being treated with liquid formulations of ABC, initiation with once-daily ABC is not generally recommended. In older children who can be treated with tablet formulations, therapy can be initiated with once-daily administration. In clinically stable patients who have undetectable viral loads and stable CD4 T lymphocyte counts while receiving the liquid formulation of ABC twice daily, the ABC dose can be changed from twice daily to once daily with the liquid or tablet formulations (see text below).</li></ul>	<table><tr><th>Metabolism/Elimination</th></tr><tr><td><ul style="list-style-type: none"><li>• ABC is systemically metabolized by alcohol dehydrogenase and glucuronyl transferase.</li><li>• The majority of ABC is excreted as metabolites in urine.</li></ul></td></tr><tr><td><p><b>Abacavir Dosing in Patients With Hepatic Impairment</b></p><ul style="list-style-type: none"><li>• ABC requires a dose adjustment in patients with mild hepatic insufficiency and is contraindicated with moderate or severe hepatic insufficiency.</li><li>• <b>Do not use</b> Epzicom, Triumeq PD, or Triumeq (or the generic equivalents of these FDC tablets) in patients with impaired hepatic function, because the dose of ABC cannot be adjusted.</li></ul></td></tr><tr><td><p><b>Abacavir Dosing in Patients With Renal Impairment</b></p><ul style="list-style-type: none"><li>• ABC does not require dose adjustment in patients with renal impairment.</li><li>• <b>Do not use</b> FDC tablets containing 3TC (Epzicom, Triumeq PD, Triumeq, or the generic equivalents of these FDC tablets) in patients with creatinine clearance &lt;30 mL/min or patients on dialysis, because the doses of 3TC cannot be adjusted. Data from FDC DTG/3TC (Dovato) suggest that patients with a sustained creatinine clearance 30–49 mL/min may experience a higher 3TC exposure and should be monitored for hematologic toxicities and potential FDC discontinuation and subsequent adjustment of the treatment regimen. See package inserts for additional information.</li></ul></td></tr></table>	Metabolism/Elimination	<ul style="list-style-type: none"><li>• ABC is systemically metabolized by alcohol dehydrogenase and glucuronyl transferase.</li><li>• The majority of ABC is excreted as metabolites in urine.</li></ul>	<p><b>Abacavir Dosing in Patients With Hepatic Impairment</b></p> <ul style="list-style-type: none"><li>• ABC requires a dose adjustment in patients with mild hepatic insufficiency and is contraindicated with moderate or severe hepatic insufficiency.</li><li>• <b>Do not use</b> Epzicom, Triumeq PD, or Triumeq (or the generic equivalents of these FDC tablets) in patients with impaired hepatic function, because the dose of ABC cannot be adjusted.</li></ul>	<p><b>Abacavir Dosing in Patients With Renal Impairment</b></p> <ul style="list-style-type: none"><li>• ABC does not require dose adjustment in patients with renal impairment.</li><li>• <b>Do not use</b> FDC tablets containing 3TC (Epzicom, Triumeq PD, Triumeq, or the generic equivalents of these FDC tablets) in patients with creatinine clearance &lt;30 mL/min or patients on dialysis, because the doses of 3TC cannot be adjusted. Data from FDC DTG/3TC (Dovato) suggest that patients with a sustained creatinine clearance 30–49 mL/min may experience a higher 3TC exposure and should be monitored for hematologic toxicities and potential FDC discontinuation and subsequent adjustment of the treatment regimen. See package inserts for additional information.</li></ul>											
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<p><b>Weight-Band Dosing of ABC Tablets for Children and Adolescents Weighing ≥14 kg and &lt;25 kg</b></p> <table><tr><th rowspan="2">Weight</th><th colspan="3">Scored 300-mg ABC Tablet</th></tr><tr><th>Twice-Daily Dose, AM</th><th>Twice-Daily Dose, PM</th><th>Once-Daily Dose</th></tr><tr><td><b>14 kg to &lt;20 kg</b></td><td>½ tablet (150 mg)</td><td>½ tablet (150 mg)</td><td>1 tablet (300 mg)</td></tr><tr><td><b>≥20 kg to &lt;25 kg</b></td><td>½ tablet (150 mg)</td><td>1 tablet (300 mg)</td><td>1½ tablets (450 mg)</td></tr></table>	Weight	Scored 300-mg ABC Tablet			Twice-Daily Dose, AM	Twice-Daily Dose, PM	Once-Daily Dose	<b>14 kg to &lt;20 kg</b>	½ tablet (150 mg)	½ tablet (150 mg)	1 tablet (300 mg)	<b>≥20 kg to &lt;25 kg</b>	½ tablet (150 mg)	1 tablet (300 mg)	1½ tablets (450 mg)	
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<p><b>Child and Adolescent (Weighing ≥25 kg) and Adult Dose</b></p> <ul style="list-style-type: none"><li>• ABC 300 mg twice daily or ABC 600 mg once daily</li></ul> <p><b>[Epzicom] Abacavir/Lamivudine</b></p> <p><i>Child and Adolescent (Weighing ≥25 kg) and Adult Dose</i></p> <ul style="list-style-type: none"><li>• One tablet once daily</li></ul>																

**[Triumeq PD] Abacavir/Dolutegravir (DTG)/Lamivudine (3TC)***Child Weighing  $\geq 10$  kg to  $< 25$  kg*

- Dispersible Triumeq PD tablets are FDA approved for children weighing  $\geq 10$  to  $< 25$  kg. Triumeq PD is not recommended for children weighing  $\geq 25$  kg who are eligible for adult Triumeq dosing.
- Administer the appropriate number of tablets once daily dispersed in 20 mL of water. See Special Instructions. Triumeq PD tablets should not be swallowed whole, chewed, cut, or crushed.

**Weight-Band Dosing of Triumeq PD Tablets for Children Weighing  $\geq 10$  kg and  $< 25$  kg**

Weight	Recommended Daily Dose	Number of Triumeq PD Tablets
10 kg to $< 14$ kg	ABC 240 mg, DTG 20 mg, 3TC 120 mg	4
14 kg to $< 20$ kg	ABC 300 mg, DTG 25 mg, 3TC 150 mg	5
20 kg to $< 25$ kg	ABC 360 mg, DTG 30 mg, 3TC 180 mg	6

- For use in children who are antiretroviral (ARV) naive or ARV experienced (but integrase strand transfer inhibitor-naive) and who are not being treated with uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1) or cytochrome P450 (CYP450) 3A inducers.

**[Triumeq] Abacavir/Dolutegravir/Lamivudine***Child and Adolescent (Weighing  $\geq 25$  kg) and Adult Dose*

- One tablet once daily
- This FDC tablet can be used in patients who are antiretroviral (ARV)-naive or ARV-experienced (but integrase strand transfer inhibitor-naive) and who are not being treated with other drugs that act as UGT1A1 or CYP450 3A inducers.

## Drug Interactions

Additional information about drug interactions is available in the [Adult and Adolescent Antiretroviral Guidelines](#) and the [HIV Drug Interaction Checker](#).

- Abacavir (ABC) neither inhibits nor is metabolized by hepatic cytochrome P450 enzymes. Therefore, it does not cause significant changes in the clearance of agents that are metabolized

through these pathways, such as protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors.

- ABC plasma concentrations can decrease when ABC is used concurrently with the ritonavir-boosted PIs atazanavir/ritonavir, lopinavir/ritonavir (LPV/r), and darunavir/ritonavir.<sup>1-3</sup> The mechanism and the clinical significance of the drug interactions with these PIs are unknown. Currently, no recommendations exist for dose adjustments when ABC is coadministered with one of these boosted PIs.
- In the pooled analysis of 230 African children with HIV with a median age of 2.1 years (range 0.1–12.8) and a median weight of 9.8 kg (range 2.5–30.0), the population pharmacokinetics of ABC showed that children on LPV/r or efavirenz had similar ABC exposures, while concomitant tuberculosis treatment and use of super-boosting with lopinavir significantly reduced ABC concentrations.<sup>4</sup>
- Alcohol exposure (0.7 g per kg ethanol, which is equivalent to five alcoholic drinks) interferes with ABC metabolism; it affects the activity of alcohol dehydrogenase and glucuronyl transferase. This interference increased ABC area under the curve (AUC) plasma exposure by 41% in adult men with HIV who received ABC 600 mg daily.<sup>5</sup>
- ABC oral solution contains sorbitol, which decreased the exposure of lamivudine (3TC) oral solution in adults when the drugs were administered concurrently.<sup>6</sup>

## Major Toxicities

- *More common:* Nausea, vomiting, fever, headache, diarrhea, rash, anorexia
- *Less common (more severe):* Serious and sometimes fatal hypersensitivity reactions (HSRs) have been observed in approximately 5% of adults and children (the rate varies by race/ethnicity) receiving ABC. HSRs generally occur during the first 6 weeks of therapy, but they have also been reported after a single dose of ABC. The risk of an ABC HSR is associated with the presence of the HLA-B\*5701 allele; the risk is greatly reduced by not using ABC in those who test positive for the HLA-B\*5701 allele. The HSR to ABC is a multiorgan clinical syndrome usually characterized by rash, or signs or symptoms in two or more of the following groups:
  - Fever
  - Constitutional symptoms, including malaise, fatigue, or achiness
  - Gastrointestinal signs and symptoms, including nausea, vomiting, diarrhea, or abdominal pain
  - Respiratory signs and symptoms, including dyspnea, cough, or pharyngitis
  - Laboratory and radiologic abnormalities, including elevated liver function tests, elevated creatine phosphokinase, elevated creatinine, lymphopenia, and pulmonary infiltrates. Lactic acidosis and severe hepatomegaly with steatosis—including fatal cases—also have been reported. Pancreatitis with laboratory abnormalities can occur.

If an HSR is suspected, ABC **should be stopped immediately and not restarted because hypotension and death may occur upon rechallenge.**

- *Rare:* Increased levels of liver enzymes, elevated blood glucose levels, elevated triglycerides (see cardiovascular risk below). Pancreatitis, lactic acidosis, and severe hepatomegaly with steatosis—including fatal cases—have been reported.

- *Rare:* Drug reaction (or rash) with eosinophilia and systemic symptoms (DRESS) syndrome.
- *Rare:* Several observational cohort studies suggest that an increased risk of myocardial infarction exists in adults who are currently using ABC or who have recently used ABC; however, other studies have not substantiated this finding, and no prospective data are available on the cardiovascular risks associated with ABC use in children. One cohort study of South African adolescents (in which 385 participants had HIV and 63 participants were HIV-negative controls) with a median age of 12 years reported an association between ABC exposure and insulin resistance, which was evaluated using homeostatic model assessment. These findings suggest that the use of ABC may be a cardiovascular risk factor for young people with perinatally acquired HIV.<sup>7</sup>

## Resistance

The International Antiviral Society–USA (IAS–USA) maintains a [list of updated HIV drug resistance mutations](#), and the [Stanford University HIV Drug Resistance Database](#) offers a discussion of each mutation.

## Pediatric Use

### *Approval*

ABC is approved by the U.S. Food and Drug Administration (FDA) for use in children with HIV aged  $\geq 3$  months as part of the nucleoside reverse transcriptase inhibitor (NRTI) component of antiretroviral therapy (ART). The World Health Organization (WHO), however, provides dosing guidance for ABC as a component of the NRTI backbone for full-term neonates starting at birth and weighing  $\geq 2$  kg (see Annex 1: Dosages for ARV Drugs in the WHO [Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery, and Monitoring](#)). The WHO guidance for ABC dosing in neonates increases the choices of antiretroviral (ARV) agents for the management of newborns in special situations where stock outs of nevirapine or zidovudine (ZDV) may affect the ability to effectively provide postnatal prophylaxis or treatment of neonatal HIV. The WHO recommendation of ABC dosing for infants starting at 1 month of age is based on the inclusion of ABC as a preferred NRTI component of the first- and second-line ARV regimens for children in the WHO [Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery, and Monitoring](#). This recommendation also takes into account the availability of the President’s Emergency Plan for AIDS Relief (PEPFAR) tentatively approved pediatric generic ABC formulations—including coformulations that include 3TC—and the cost of ARV drugs in resource-limited settings.

## Efficacy

Both the once-daily and twice-daily doses of ABC have demonstrated durable antiviral efficacy in pediatric clinical trials that is comparable to the efficacy observed for other NRTIs in children.<sup>8-12</sup>

## Pharmacokinetics

### *Pharmacokinetics in Neonates and Infants*

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1106 trial reported PK data in 25 infants with HIV aged <3 months, who were initiated on a median ABC dose of 10 mg/kg (range, 6–13 mg/kg) twice daily in combination with lamivudine and LPV/r after 1 month of life. Median age was 6 weeks (range, 1.5–11 weeks); median weight was 2,250 g (range 1,360–3,320 g); median gestational age was 36 weeks (range, 27–39 weeks). Sparse and pre-dose PK ABC samples were repeatedly obtained throughout 24 weeks of study follow-up. ABC plasma exposures were high compared to the published data in infants aged >3 months and decreased rapidly between 2 and 8 months of age as the infants matured and ABC clearance increased.<sup>13</sup> In the Tygerberg cohort study from South Africa, 10 healthy term neonates at the median postnatal age of 10 days (range 6–15), who were administered a single ABC dose of 8 mg/kg/dose before 15 days of life, had substantially higher exposures than those reported in infants and children and no reported adverse events.<sup>14</sup> ABC exposure also was higher in neonates compared to infants and children, likely due to slower drug clearance through immature enzyme pathways in neonates.

PK modeling of ABC starting at birth has been conducted using pooled data from 308 ABC concentration measurements obtained from three studies administering ABC liquid to 45 young infants (including 21 full-term neonates <15 days of age with intensive PK).<sup>15</sup> Two of these studies, the Pediatric AIDS Clinical Trials Group (PACTG) 321 study and the Tygerberg cohort, performed intensive PK sampling in full-term neonates receiving ABC for HIV prophylaxis. The third study, IMPAACT P1106 described above, performed sparse PK sampling on full-term and low-birth weight (LBW; <2,500 g) infants with HIV. LBW infants were older at the first PK assessment, with a median postnatal age of 73 days (range 41–190) and weight of 3.8 kg (range 2.4–5.8). ABC PK parameters in neonates were estimated using PK simulations to achieve plasma ABC exposures ( $AUC_{0-12}$ ) within the expected adult range (3.2–25.2 mcg•hr/mL). The PK model predicted a slow ABC clearance of 2.51 mL/min per kg at birth, which doubled by 4 weeks of age. Simulations predicted that an ABC dose of 2 mg/kg twice daily in full-term neonates from birth to <4 weeks and an ABC dose of 4 mg/kg twice daily in infants aged 4 to 12 weeks would achieve target  $AUC_{0-12}$ ; however, data in LBW infants are lacking.<sup>15</sup> Based on these data, the weight-band dosing of ABC for neonates has been developed for neonates from birth to age <1 month and is included in the [WHO Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery, and Monitoring](#) Annex 1: Dosages for ARV Drugs.<sup>16</sup> This weight-band dosing for neonates approximates the ABC dosing per kg based on the postnatal age (see Table 1 below).



**Table 1. Simplified Weight-Band Dosing for Full-Term Neonates from Birth to <1 Month of Age (WHO [Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery, and Monitoring](#) Annex 1: Table A1.4)**

Birth to <1 Month of Age		
Weight	Volume of ABC Oral Solution 20 mg/mL Twice Daily <sup>a,b</sup>	ABC Dose in mg Twice Daily (ranges mg/kg, from lowest to highest weight within the weight band) <sup>a,b</sup>
2 kg to <3 kg	0.4 mL	8 mg (4.0–2.8 mg/kg)
3 kg to <4 kg	0.5 mL	10 mg (3.3–2.6 mg/kg)
4 kg to < 5 kg	0.6 mL	12 mg (3.0–2.4 mg/kg)

<sup>a</sup> Simplified weight-band dosing exceeds recommended mg/kg ABC dosing in neonates and infants.

<sup>b</sup> Neonatal ABC dose is based on birth weight and does not require weight-based adjustment during the first month of life.

Key: ABC = Abacavir

For infants aged  $\geq 1$  month with weight 3 to <6 kg, the WHO [Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery, and Monitoring](#) currently recommend a twice-daily dose of 3 mL (60 mg) of ABC 20 mg/mL solution (range 20.0–10.2 mg/kg). The weight-band dosing for neonates and infants within the WHO HIV guidelines is higher than the modeled weight-based dosing for practical considerations in resource-limited settings. As new, generic pediatric formulations of ABC become available in resource-limited settings, there is potential for the revision of the WHO guidelines for weight-band dosing of ABC for young infants.

Based on the PK modeling from three infant studies<sup>15</sup> and the neonatal and infant safety data from the IMPAACT 1106 study and two observational cohort studies (see Safety in Neonates and Infants below), the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV recommends an ABC dose of 2 mg/kg twice daily for neonates from birth to <1 month of age and an ABC dose of 4 mg/kg twice daily for full-term infants aged  $\geq 1$  month and <3 months.

## Pharmacokinetics in Children

PK studies of ABC in children aged <12 years have demonstrated that metabolic clearance of ABC in adolescents and young adults (aged 13–25 years) is slower than that observed in younger children and approximates clearance seen in older adults.<sup>17</sup>

The PKs of ABC administered once daily in children with HIV aged 3 months through 12 years were evaluated in three crossover, open-label PK trials of twice-daily versus once-daily dosing of ABC and 3TC (PENTA 13 [n = 14], PENTA 15 [n = 18], and ARROW [n = 36]).<sup>5,18-21</sup> The data from these three pediatric trials were used to develop a model for ABC PKs; this model predicted that systemic plasma ABC exposure after once-daily dosing would be equivalent to the exposure seen after twice-daily dosing in infants and children aged  $\leq 12$  years.<sup>18-22</sup> Both these trials and PK modeling have demonstrated that once-daily dosing with either the tablet or the liquid formulation of ABC produces plasma exposures comparable to those seen with a twice-daily dosing schedule that uses the same total daily dose of ABC.<sup>5</sup>

## Dosing

### *Dosing and Formulations*

Initially, the recommended dose for pediatric use was ABC 8 mg/kg twice daily for a total of 16 mg/kg per day. A 2015 FDA review suggested that a total daily dose of ABC 600 mg could be used safely in a person weighing 25 kg (i.e., ABC 24 mg/kg per day, a 50% increase from the previously recommended dose). The weight-band dosing table recommends total daily doses as high as ABC 21.5 mg/kg per day to ABC 22.5 mg/kg per day when treating patients with the tablet formulation.<sup>5</sup> No difference is seen in the ABC peak plasma concentration ( $C_{max}$ ) and AUC for the ABC liquid formulation compared to the tablet formulation.<sup>23</sup> Doses of the liquid ABC formulation are similar to those used for weight-band dosing with tablet formulations and should be considered for use in younger children who are unable to swallow a pill.

In the three ABC dosing pediatric trials described above,<sup>18-21</sup> only children who had low viral loads and who were clinically stable on the twice-daily dose of ABC were eligible to change to once-daily ABC dosing. Efficacy data from a 48-week follow-up in the ARROW trial demonstrated clinical non-inferiority of once-daily ABC (n = 336) versus twice-daily ABC (n = 333) in tablet form combined with a once-daily or twice-daily 3TC-based ARV regimen.<sup>12</sup> To date, no clinical trials have been conducted involving children who initiated therapy with once-daily dosing of the ABC liquid formulation. In children who can be treated with pill formulations, initiating therapy with once-daily dosing of ABC at a dose of 16 mg/kg (with a maximum dose of ABC 600 mg) is recommended. However, twice-daily dosing is recommended for infants and young children who initiate therapy with the liquid formulation of ABC. Switching to once-daily dosing with the liquid or pill formulation could be considered in clinically stable children with suppressed viral loads and stable CD4 T lymphocyte counts.

## Toxicity

### *Safety in Neonates and Infants*

Data from the PACTG 321, the IMPAACT P1106 trial, and two observational European and African cohorts provided reassuring data on the safety of ABC in infants when initiated at <3 months of age, including infants with weight <3 kg.<sup>13,24,25</sup> The IMPAACT P1106 trial reported 24 weeks of safety data in 27 infants in whom repeated dosing of ABC was initiated at the median age of 60 days. Fifteen infants (55.6%; 90% CI, 38.3–72.0) met the safety endpoint of death or a Grade 3 or higher adverse event (AE). None of the AEs were related to ABC, and none led to interruptions or adjustments of ABC dosing. No hypersensitivity reactions were reported with the multidose treatment.<sup>13</sup> In two cohorts of neonates (<1 months of age) who received a single ABC dose, ABC was well tolerated; all reported AEs in the PACTG 321 study were unrelated to ABC, and no AEs were reported in the Tygerberg cohort.<sup>14,26</sup> The European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC) reported safety outcomes among 139 children from 13 cohorts in 11 countries in Europe who initiated ABC at age <3 months. By 12 months on ABC, 3.6% (n = 4) had discontinued ABC because of an ART safety concern and 11.8% (n = 15) discontinued ABC for any reason.<sup>24</sup> Another observational study of nine cohorts from the International Epidemiology Databases to Evaluate AIDS (IeDEA) Southern Africa collaboration compared safety outcomes between infants who started ABC aged <28 days (n = 96) and those aged ≥28 days (n = 835), and between infants who started ABC with weight <3 kg (n = 246) and those with weight ≥3 kg



(n = 53).<sup>25</sup> ABC discontinuations at 6 and 12 months were not significantly different in infants who started ART aged <28 days and ≥28 days or in infants who weighed <3 kg and ≥3 kg.<sup>25</sup>

ABC has less of an effect on mitochondrial function than the NRTI ZDV<sup>8,9</sup> and less bone and renal toxicity than tenofovir disoproxil fumarate.<sup>27,28</sup>

Recent systemic review and meta-analysis of the 54 full-text articles on the observational and experimental studies conducted in infants, children, and adolescents with HIV who are aged 10 to 19 years and that included data on safety, efficacy, or both, and were published in English or French between 2009 and 2022 reported that toxic effects due to ABC use in infants, children, and adolescents remain rare and manageable.<sup>29</sup>

## References

1. Waters LJ, Moyle G, Bonora S, et al. Abacavir plasma pharmacokinetics in the absence and presence of atazanavir/ritonavir or lopinavir/ritonavir and vice versa in HIV-infected patients. *Antivir Ther.* 2007;12(5):825-830. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17713166>.
2. Pruvost A, Negredo E, Theodoro F, et al. Pilot pharmacokinetic study of human immunodeficiency virus-infected patients receiving tenofovir disoproxil fumarate (TDF): investigation of systemic and intracellular interactions between TDF and abacavir, lamivudine, or lopinavir-ritonavir. *Antimicrob Agents Chemother.* 2009;53(5):1937-1943. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19273671>.
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