

## Bictegravir (BIC)

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### Summary

- No dose adjustment for bictegravir (BIC) is recommended in pregnancy.
- First-trimester exposure to BIC has not been associated with an increased risk of congenital anomalies.

### Human Studies in Pregnancy

#### Pharmacokinetics

BIC pharmacokinetics (PK) during pregnancy have been reported in two clinical studies,<sup>1,2</sup> a case series,<sup>3,4</sup> and one case report.<sup>5</sup>

IMPAACT 2026<sup>6</sup> evaluated the PK of BIC among 27 pregnant women, which showed that total BIC area under the curve (AUC) was decreased by 46% to 52%; the concentrations at 24 hours postdose ( $C_{24h}$ ) were 62% to 68% lower during pregnancy compared to postpartum.<sup>1</sup> Seven of 12 (58%) participants during the second trimester and 13 of 21 (62%) during the third trimester fell below the 10th percentile AUC for nonpregnant adults, but none of these women had a detectable viral load. All  $C_{24h}$  values across the second and third trimesters were above the BIC protein-adjusted 95% maximal effective concentration ( $EC_{95}$ ) of 0.162 ug/mL, with median values approximately sevenfold and 5.9-fold above the  $EC_{95}$ .<sup>1</sup> Because BIC is highly protein bound and pregnancy can be associated with decreased plasma protein binding, unbound drug concentrations were also assessed. Compared with postpartum, the percent unbound was 45% and 42% higher in the second and third trimesters, respectively. However, median unbound BIC concentrations remained lower during pregnancy (3.83 ng/mL and 3.01 ng/mL for the second and third trimesters, respectively, compared to 5.83 ng/mL during postpartum). Virologic suppression (<40 copies/mL) was maintained in 88% to 92% of participants across pregnancy, birth, and postpartum, and no confirmed infant HIV infections occurred among the 26 for whom data are available.

A separate study<sup>2</sup> in 33 pregnant women showed that total BIC AUC was approximately 56% to 59% lower, and BIC trough concentrations ( $C_{trough}$ ) were approximately 70% to 74% lower during the second or third trimester compared to 6 or 12 weeks postpartum. Total BIC AUC in the pregnant women was 41% lower during the third trimester compared with historical data in nonpregnant adults with HIV. The AUC for unbound BIC was approximately 38% to 41% lower during pregnancy than postpartum. The mean unbound fractions were higher during pregnancy than postpartum (0.351% and 0.365% during the second and third trimester, respectively, compared with 0.261% and 0.252% at 6 and 12 weeks postpartum, respectively). Mean  $C_{trough}$  values during the second and third trimesters were about 6.5-fold above the BIC protein-adjusted  $EC_{95}$ , and all but one individual  $C_{trough}$  value was above this threshold. All women maintained virologic suppression (<50 copies/mL) through Week 18 postpartum, including at birth, and no infant HIV infections occurred.

Collectively, these findings demonstrate that despite lower AUC and  $C_{24h}$  or  $C_{trough}$  values during pregnancy, drug exposures were still above those needed to maintain virologic suppression when

using standard BIC doses, and thus no dose adjustment is recommended. Separate large cohort studies have also demonstrated rates of virologic suppression (<50 copies/mL) of approximately 82% to 91% through birth with BIC/tenofovir alafenamide/emtricitabine.<sup>7</sup>

## Placental and Breast Milk Passage

Placental transfer of BIC is high, with a mean/median umbilical cord blood-to-maternal plasma ratio of approximately 1.4 at birth.<sup>1,2</sup> The estimated median half-life in neonates based on washout data is prolonged in comparison to adults, with one study estimating 43 hours (interquartile range 38–58; n = 10)<sup>2</sup> and another estimating 33 hours (interquartile range 26–46; n = 25).<sup>1</sup> These umbilical cord blood-to-maternal plasma ratios are comparable to a previous case series in which ratios of 1.49 were measured in one patient 20 hours after BIC dosing and 1.42 in another patient 7 hours after BIC dosing.<sup>3</sup> A separate case report conveyed an umbilical cord blood-to-maternal plasma ratio of 0.68 approximately 16 hours after BIC dosing.<sup>4</sup> The concentration of BIC was 2,826 ng/mL in cord blood at birth, 2,097 ng/mL in the infant on Day 3 after birth, and undetectable (<5 ng/mL) in the infant by Day 22.

Data on the passage of BIC in human breast milk are very limited. BIC milk-to-plasma ratios have only been reported in one woman, which revealed a ratio of 0.01 and subsequent estimated infant daily dose of 0.01 mg/kg.<sup>8</sup> Additional data are needed to refine our understanding of the breast milk passage of BIC.

## Teratogenicity/Adverse Pregnancy Outcomes

The Antiretroviral Pregnancy Registry (APR) provides updated birth defect data for BIC and other antiretroviral (ARV) drugs twice a year through an [interim report](#) released in June and December. The APR has monitored sufficient numbers of first-trimester exposures to BIC to detect at least a twofold increase in the risk of overall birth defects. No such increase in the risk of birth defects has been observed with BIC. [Figure 1. Summary of Birth Defects Among First Trimester Exposures in the APR interim report](#) provides a summary of the number and prevalence of birth defects per live births among cases of first-trimester exposure to BIC and other ARV drugs reported to the APR where there are sufficient data to determine 95% confidence intervals. The data in Figure 1 can be compared with the prevalence of birth defects in the U.S. population (2.72 birth defects per 100 live births) based on the Centers for Disease Control and Prevention surveillance system (The Metropolitan Atlanta Congenital Defects Program [MACDP]) and with the Texas Birth Defects Registry ([TBDR] 4.17 per 100 live births).

Separate, smaller retrospective studies with sample sizes of approximately 50 to 150 participants have also reported pregnancy outcomes with BIC and have not identified higher rates of congenital anomalies with exposure occurring during the first trimester<sup>7,9</sup> or at any time during pregnancy.<sup>10</sup>

## Animal Studies

### Carcinogenicity

BIC has not been shown to be genotoxic or mutagenic *in vitro*.<sup>11</sup>

## **Reproduction/Fertility**

BIC did not affect fertility, reproductive performance, or embryonic viability in male or female rats at exposures (based on AUC) that were 29 times higher than those observed in humans who received the recommended dose.<sup>11</sup>

## **Teratogenicity/Adverse Pregnancy Outcomes**

No adverse embryo-fetal effects were observed in rats and rabbits at BIC exposures (based on AUC) of up to about 36 times (in rats) and 0.6 times (in rabbits) the exposures observed in humans who received the recommended dose. Spontaneous abortion, increased clinical signs (e.g., fecal changes, thin body, cold to touch), and decreased body weight were observed in rabbits at a maternally toxic dose (i.e., 1,000 mg/kg per day, which produced an exposure approximately 1.4 times higher than the exposure observed in humans who received the recommended dose).<sup>11</sup>

## **Placental and Breast Milk Passage**

No data are available on placental passage of BIC in animals. In a prenatal and postnatal development study conducted in rats, BIC was detected in the plasma of nursing rat pups on postnatal Day 10, likely due to the presence of BIC in milk.<sup>11</sup>

**Excerpt from [Table 14](#)**

**Note:** When using fixed-dose combination (FDC) tablets, refer to other sections in [Appendix B](#) and [Table 14](#) in the Perinatal Guidelines for information about the dosing and safety of individual drug components of the FDC tablet during pregnancy.

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations <sup>a</sup>	Use in Pregnancy
<p><b>Bictegravir/Emtricitabine/ Tenofovir Alafenamide</b> (BIC/FTC/TAF) <i>Biktarvy</i></p> <p><b>Note:</b> BIC is available only as part of an FDC tablet.</p>	<p><b>BIC/FTC/TAF (Biktarvy)</b></p> <ul style="list-style-type: none"> <li>• BIC 50-mg/FTC 200-mg/TAF 25-mg tablet</li> <li>• BIC 30-mg/FTC 120-mg/TAF 15-mg tablet</li> </ul>	<p><b>Pregnancy</b></p> <p><i>PK in Pregnancy</i></p> <ul style="list-style-type: none"> <li>• AUC and C<sub>24h</sub>/C<sub>trough</sub> are decreased during the third trimester compared with postpartum, but exposures during pregnancy are well above those needed to inhibit viral replication.</li> </ul> <p><i>Dosing in Pregnancy</i></p> <ul style="list-style-type: none"> <li>• No change in dose indicated</li> </ul> <p>For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., <a href="#">FTC</a>, <a href="#">TAF</a>).</p> <p><b>Standard Adult Doses</b></p> <ul style="list-style-type: none"> <li>• One tablet of BIC 50 mg/FTC 200 mg/TAF 25 mg once daily with or without food</li> </ul>	<p>High placental transfer to fetus<sup>b</sup></p> <p>No evidence of human teratogenicity (can rule out twofold increase in overall birth defects)</p> <p>BIC can be taken with food at the same time as any preparation containing iron or calcium—including prenatal vitamins—but should not be administered within 2 hours of these preparations when taken on an empty stomach. BIC can be taken at least 2 hours before or 6 hours after antacids containing aluminum or magnesium.</p>

<sup>a</sup> Individual ARV drug doses may need to be adjusted in patients with renal or hepatic insufficiency (for details, see the [Adult and Adolescent Antiretroviral Guidelines Appendix B](#)).

<sup>b</sup> Placental transfer categories are determined by mean or median cord blood-to-maternal delivery plasma drug ratio:

**High:** >0.6  
**Moderate:** 0.3–0.6  
**Low:** <0.3

**Key:** ARV = antiretroviral; AUC = area under the curve; BIC = bictegravir; C<sub>24h</sub> = concentrations at 24 hours postdose; **C<sub>trough</sub> = trough concentration**; FDC = fixed-dose combination; FTC = emtricitabine; PK = pharmacokinetics; TAF = tenofovir alafenamide

## References

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