

Bictegravir (BIC)

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Summary

- Pharmacokinetic data are insufficient to make dosing recommendations for bictegravir (BIC) during pregnancy.
- Clinical data are insufficient to characterize the risk for congenital anomalies associated with *in utero* exposure to BIC. No reproductive toxicity or teratogenicity concerns were identified in animal studies.

Human Studies in Pregnancy

Pharmacokinetics

Limited information about the pharmacokinetics (PK) of BIC in pregnancy was presented in a case series describing two pregnant women, one of which had paired PK data during pregnancy and postpartum. This patient's area under the curve (AUC), trough concentration, and maximum plasma concentration were 35%, 49%, and 19% lower, respectively, at 33 weeks gestation compared to 6 weeks postpartum. The patient remained virologically suppressed through delivery. The generalizability of these findings is currently unknown.^{1,2}

Placental and Breast Milk Passage

Data regarding placental transfer of BIC are limited and provide mixed results. Data from two patients treated with BIC during pregnancy demonstrated high placental transfer; the umbilical cord-to-maternal plasma ratio was 1.49 in one patient 20 hours after BIC dosing and 1.42 in another patient 7 hours after BIC dosing.¹ A separate case report reported an umbilical cord-to-maternal plasma ratio of 0.68 approximately 16 hours after BIC dosing.² The concentration of BIC was 2,826 ng/mL in cord blood at delivery, 2,097 ng/mL in the infant on Day 3 after birth, and undetectable (<5 ng/mL) in the infant by Day 22. However, an *ex vivo* dually perfused human cotyledon model found placental transfer was low with a median (interquartile range 25–75) maternal-to-fetal ratio of 7% (6% to 9.5%).³ Additional data are needed to refine our understanding of placental passage of BIC. No data are available on the passage of BIC in human breast milk.

Teratogenicity/Adverse Pregnancy Outcomes

The Antiretroviral Pregnancy Registry has not monitored sufficient numbers of first-trimester exposures to BIC to report on the risk of overall birth defects. Supplemental data from the Antiretroviral Pregnancy Registry on central nervous system (CNS) birth defect outcomes in 234 live births to women who were exposed to BIC during periconception, or pregnancy reported two infants with CNS birth defects; 2 of 165 infants with periconception exposure, 0 of 18 infants with later first-trimester exposure, and 0 of 51 infants with exposure in the second or third trimester. None of the CNS defects was a neural tube defect; no encephalocele defects were reported. These data are insufficient to make conclusions regarding the safety of BIC during pregnancy.⁴

Animal Studies

Carcinogenicity

BIC has not been shown to be genotoxic or mutagenic *in vitro*.⁵

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.⁵

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).⁵

Placental and Breast Milk Passage

No data are available on placental passage of BIC. 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.⁵

Excerpt from [Table 14](#)

Note: When using 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 ^a	Use in Pregnancy
<p>Bictegravir/Emtricitabine/ Tenofovir Alafenamide (BIC/FTC/TAF) <i>Biktarvy</i></p> <p>Note: BIC is available only as part of an FDC tablet.</p>	<p>BIC/FTC/TAF (Biktarvy)</p> <ul style="list-style-type: none"> • BIC 50-mg/FTC 200-mg/TAF 25-mg tablet • BIC 30-mg/FTC 120-mg/TAF 15-mg tablet 	<p>Pregnancy <i>PK in Pregnancy</i></p> <ul style="list-style-type: none"> • No PK studies in human pregnancy <p><i>Dosing in Pregnancy</i></p> <ul style="list-style-type: none"> • Insufficient data to make dosing recommendations <p>For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., FTC, TAF).</p> <p>Standard Adult Doses</p> <ul style="list-style-type: none"> • One tablet of BIC 50-mg/FTC 200-mg/TAF 25-mg once daily with or without food 	<p>More data are needed to characterize the placental passage of BIC.</p> <p>Insufficient data exist to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits exists.</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>

^a 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, Table 11](#)).

Key: ARV = antiretroviral; BIC = bictegravir; FDC = fixed-dose combination; FTC = emtricitabine; PK = pharmacokinetics; TAF = tenofovir alafenamide

References

1. Bukkems VE, Hidalgo-Tenorio C, Garcia C, et al. First pharmacokinetic data of bictegravir in pregnant women living with HIV. *AIDS*. 2021;35(14):2405-2406. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34723856>.
2. Le MP, Ferre VM, Mazy F, et al. Bictegravir pharmacokinetics in a late-presenting HIV-1-infected pregnant woman: a case report. *J Antimicrob Chemother*. 2022;77(3):851-853. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34792155>.
3. Pencole L, Le MP, Bouchet-Crivat F, Duro D, Peytavin G, Mandelbrot L. Placental transfer of the integrase strand inhibitors cabotegravir and bictegravir in the ex-vivo human cotyledon perfusion model. *AIDS*. 2020;34(14):2145-2149. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32796211>.
4. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral pregnancy registry international interim report for 1 January 1989–31 January 2022. Wilmington, NC: Registry Coordinating Center; 2022. Available at: http://www.apregistry.com/forms/interim_report.pdf.
5. Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide) [package insert]. Food and Drug Administration. 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/210251Orig1s015ltr.pdf.