

## ***Bictegravir (BIC)***

(Last updated December 30, 2021; last reviewed December 30, 2021)

### **Animal Studies**

#### *Carcinogenicity*

Bictegravir (BIC) has not been shown to be genotoxic or mutagenic *in vitro*.<sup>1</sup>

#### *Reproduction/Fertility*

BIC did not affect fertility, reproductive performance, or embryonic viability in male and female rats at exposures (based on area under the curve [AUC]) that were 29 times higher than those observed in humans who received the recommended dose.<sup>1</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>1</sup>

#### *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.<sup>1</sup>

### **Human Studies in Pregnancy**

#### *Pharmacokinetics*

Limited information about the pharmacokinetics (PKs) of BIC in pregnancy are presented in a case series describing two pregnant individuals of whom one had PK data during pregnancy and postpartum. This patient's AUC,  $C_{\text{trough}}$ , and  $C_{\text{max}}$  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 unknown at this time.<sup>2</sup>

#### *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.<sup>2</sup> However, placental transfer was found to be low in an *ex vivo* dually perfused human cotyledon model with a median (interquartile range 25–75) maternal-to-fetal ratio of 7% (6% to 9.5%).<sup>3</sup> Additional data are needed to refine our understanding of placental passage of BIC. No data are available on breast milk passage of BIC in humans.

### *Teratogenicity/Adverse Pregnancy Outcomes*

The Antiretroviral Pregnancy Registry has prospectively monitored 140 pregnancies in women treated with BIC during periconception or pregnancy, including 91 infants with periconception exposure, 9 infants with later first-trimester exposure, and 40 infants with exposure in the second or third trimester. Three birth defects, including one central nervous system defect that was not a neural tube defect or encephalocele, have been reported to date. However, these data are insufficient to make conclusions regarding the safety of BIC during pregnancy.<sup>4</sup>

## Excerpt from Table 11

**Note:** When using fixed-dose combination (FDC) tablets, refer to other sections in [Appendix B](#) and [Table 11](#) in the Perinatal Guidelines for information about the dosing and safety of individual drug components of the FDC tablet during pregnancy.

| Generic Name<br>(Abbreviation)<br>Trade Name   | Formulation   | Dosing Recommendations <sup>a</sup>  | Use in Pregnancy  |
|--|---|--|---|
| <p><b>Bictegravir/Emtricitabine/<br/>Tenofovir Alafenamide</b><br/>(BIC/FTC/TAF)<br/><i>Biktarvy</i></p> <p><b>Note:</b> BIC is available only as part of an FDC tablet.</p> | <p><b>BIC/FTC/TAF<br/>(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>Standard Adult Doses</b></p> <ul style="list-style-type: none"> <li>One tablet of BIC 50 mg/FTC 200 mg/TAF 25 once daily with or without food</li> </ul> <p><b>Pregnancy</b><br/><i>PK in Pregnancy</i></p> <ul style="list-style-type: none"> <li>No PK studies in human pregnancy</li> </ul> <p><i>Dosing in Pregnancy</i></p> <ul style="list-style-type: none"> <li>Insufficient data to make dosing recommendations</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>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> |

<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, Table 11](#)).

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

## References

1. Biktarvy (bictegravir, emtricitabine, tenofovir alafenamide fumarate) [package insert]. Food and Drug Administration. 2021. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/210251s010lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/210251s010lbl.pdf).
2. 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>.
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 2021. Wilmington, NC: Registry Coordinating Center. 2021. Available at: <http://www.apregistry.com>.