

Tenofovir Alafenamide (Vemlidy, TAF)

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Tenofovir alafenamide (TAF) is an orally bioavailable form of tenofovir (TFV). For information about tenofovir disoproxil fumarate (TDF), see the [TDF section](#).

Animal Studies

Carcinogenicity

Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are both prodrugs of tenofovir (TFV). TAF is converted rapidly to TFV, and TFV exposure in rats and mice is lower after TAF administration than TDF administration. Carcinogenicity studies for TFV were performed with TDF, but given the lower TFV exposure with TAF, the associated carcinogenicity is assumed to be commensurate or lower. Long-term oral carcinogenicity studies of TFV in mice and rats were carried out at TFV exposures that were 167 times (in mice) and 55 times (in rats) the TFV exposures observed in humans who received the recommended doses of TAF. In female mice, liver adenomas were increased.^{1,2}

Reproduction/Fertility

Reproduction studies have been performed at TAF exposures that in rats were similar to and in rabbits were 53 times higher than the exposure seen in humans who received the recommended dose. These studies revealed no evidence of impaired fertility or mating performance associated with TAF administration.^{1,2}

Teratogenicity/Adverse Pregnancy Outcomes

No effects on early embryonic development were seen when TAF was administered to male or female rats at doses that produced exposures that were 62 times the exposure seen in humans who received the therapeutic dose.^{1,2}

Placental and Breast Milk Passage

Rat studies demonstrated secretion of TFV in breast milk after administration of TDF, but whether TAF is present in animal milk is not known.¹

Human Studies in Pregnancy

Pharmacokinetics

The pharmacokinetics (PK) of TAF were evaluated in 31 women who were taking TAF 25 mg without a PK enhancer and in 27 women who were taking TAF 10 mg boosted with cobicistat (COBI)³ 150 mg. This study evaluated plasma TAF exposures with and without boosting in pregnant and postpartum women relative to nonpregnant adults and did not find significant differences in the PK between pregnant and postpartum women who were taking TAF 10 mg boosted with COBI. The study did find, however, that although pregnant women who were taking unboosted TAF had plasma TAF exposures similar to those observed in nonpregnant adults, the TAF exposures in these women increased significantly during the postpartum period. Another report described TAF PK in 17 women who were taking TAF 25 mg boosted with either COBI or ritonavir; plasma exposures for TAF during pregnancy were similar to those seen postpartum.⁴

Placental and Breast Milk Passage

Very limited data exist on the TAF levels in placental and breast milk. One study found that TAF was below the assay limit of quantification (<3.9 ng/mL) in 15 of 15 cord blood samples tested; intracellular TFV diphosphate was not measured in the cord blood or the samples of maternal plasma at delivery, and maternal plasma TAF concentrations at delivery were measurable in only 2 of the 15 paired samples.³ No data are available on the breast milk passage of TAF in humans.

Teratogenicity/Adverse Pregnancy Outcomes

The data from the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) 2010, a randomized trial of dolutegravir (DTG) containing ART regimens in pregnancy, found lower composite adverse outcomes in the group receiving DTG+FTC/TAF (TAF with emtricitabine and dolutegravir) than in the group receiving DTG+FTC/TDF (TDF with emtricitabine and dolutegravir) or EFV+FTC/TDF (TDF with efavirenz and emtricitabine), although it is noteworthy that the DTG+FTC/TAF arm of the trial had higher maternal weight gain than the other two arms and an increased risk of stillbirth compared with the arm receiving EFV+FTC/TDF (3.7% vs. 1.9%).⁵

The Antiretroviral Pregnancy Registry has monitored sufficient numbers of first-trimester exposures to TAF to detect at least a twofold increase in the risk of overall birth defects. However, no such increase in the risk of birth defects has been observed with TAF. Among the cases of first-trimester TAF exposure that have been reported to the Antiretroviral Pregnancy Registry, the prevalence of birth defects was 4.9% (17 of 349 live births; 95% confidence interval, 2.9% to 7.7%) compared with a 2.7% total prevalence in the U.S. population, according to the Centers for Disease Control and Prevention birth defects surveillance system MACDP (Metropolitan Atlanta Congenital Defects Program). The data reflect a modest but statistically significant increase in the rate of overall defects for TAF compared with MACDP, but this increase was not observed in comparison with the 4.17% prevalence of overall defects reported in the Texas Birth Defects Registry. No pattern was found in the reported birth defects, and the clinical significance of these findings has not been determined.⁶

Excerpt from Table 10

Note: When using FDC tablets, refer to other sections in Appendix B and Table 10 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
Tenofovir Alafenamide (TAF) <i>Vemlidy</i>	TAF (Vemlidy) <i>Tablet:</i> • 25 mg	Standard Adult Doses <i>TAF (Vemlidy):</i> • One tablet once daily with food	Low placental transfer to fetus. ^b
(TAF/BIC/FTC) <i>Biktarvy</i>	TAF/BIC/FTC (Biktarvy): • TAF 25 mg/BIC 50 mg/FTC 200 mg tablet	<i>TAF/BIC/FTC (Biktarvy):</i> • One tablet once daily with or without food	Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats.
(TAF/FTC) <i>Descovy</i>	TAF/FTC (Descovy): • TAF 25 mg/FTC 200 mg tablet	<i>TAF/FTC (Descovy):</i> • One tablet once daily with or without food	Renal function should be monitored because of the potential for renal toxicity.
(TAF/EVG/c/FTC) <i>Genvoya</i>	TAF/EVG/c/FTC (Genvoya): • TAF 10 mg/EVG 150 mg/COBI 150 mg/FTC 200 mg tablet	<i>TAF/EVG/c/FTC (Genvoya):</i> • One tablet once daily with food	
(TAF/FTC/RPV) <i>Odefsey</i>		<i>TAF/FTC/RPV (Odefsey):</i> • One tablet once daily with food	
(TAF/DRV/c/FTC) <i>Symtuza</i>			

	<p>TAF/FTC/RPV (Odefsey):</p> <ul style="list-style-type: none"> TAF 25 mg/FTC 200 mg/RPV 25 mg tablet <p>TAF/DRV/c/FTC (Symtuza):</p> <ul style="list-style-type: none"> TAF 10 mg/DRV 800 mg/COBI 150 mg/FTC 200 mg tablet 	<p><i>TAF/DRV/c/FTC (Symtuza):</i></p> <ul style="list-style-type: none"> One tablet once daily with food <p>Pregnancy</p> <p><i>PKs in Pregnancy:</i></p> <ul style="list-style-type: none"> Plasma PKs not significantly altered in pregnancy. <p><i>Dosing in Pregnancy:</i></p> <ul style="list-style-type: none"> No change in dose indicated. <p>For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., BIC, COBI, DRV, EVG, FTC, RPV).</p>	
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^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 10](#)).

^b Placental transfer categories are determined by mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6

Moderate: 0.3–0.6

Low: <0.3

Key: ARV = antiretroviral; BIC = bictegravir; COBI = cobicistat; DRV/c = darunavir/cobicistat; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; PK = pharmacokinetic; RPV = rilpivirine; TAF = tenofovir alafenamide

References

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2. Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (Genvoya) [package insert]. Food and Drug Administration. 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/207561s023lbl.pdf.
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6. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 January 2020. Wilmington, NC: Registry Coordinating Center. 2020. Available at: <http://www.apregistry.com>.