



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Elvitegravir (Vitekta, EVG)

(Last updated October 26, 2016; last reviewed October 26, 2016)

Elvitegravir is classified as Food and Drug Administration Pregnancy Category B.

Animal Studies

Carcinogenicity

Elvitegravir was not genotoxic or mutagenic *in vitro*. No carcinogenicity was detected in long-term studies in mice at exposures up to 14-fold and rats at exposures up to 27-fold that achieved with human systemic exposure at the recommended dose.¹

Reproduction/Fertility

Elvitegravir did not affect fertility in male and female rats at approximately 16- and 30-fold higher exposures than in humans at standard dosing. Fertility was normal in offspring.¹

Teratogenicity/Developmental Toxicity

Studies in rats and rabbits have shown no evidence of teratogenicity or effect on reproductive function with elvitegravir.¹

Placental and Breast Milk Passage

No data on placental passage are available for elvitegravir. Studies in rats have demonstrated that elvitegravir is secreted in breast milk.

Human Studies in Pregnancy

Pharmacokinetics

Pharmacokinetic (PK) studies of elvitegravir in human pregnancy are limited to a single case report of elvitegravir and cobicistat PK, safety, and efficacy in a single pregnant woman. Elvitegravir and cobicistat pharmacokinetics were assessed in this woman at 34 weeks' gestation and repeated at 6 weeks postpartum. Elvitegravir area under the curve (AUC) was similar during pregnancy and postpartum, but C_{min} was reduced by 60% during pregnancy compared to postpartum (and was below the suggested target concentration of 0.13 mg/L). Cobicistat AUC was reduced by 44% during pregnancy compared to postpartum. Despite the low elvitegravir C_{min} , viral load remained undetectable throughout the pregnancy.²

Placental and Breast Milk Passage

The only data available on placental passage of elvitegravir in humans are from the single case report cited above. At delivery, maternal and cord blood plasma elvitegravir concentrations were both 0.30 mg/L.² No data are available on human breast milk transfer of elvitegravir.

Teratogenicity/Developmental Toxicity

In the Antiretroviral Pregnancy Registry, insufficient numbers of first-trimester exposures to elvitegravir in humans have been monitored to be able to make a risk determination.³

Excerpt from Table 8^a

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Use in Pregnancy															
Elvitegravir (EVG) <i>Vitekta</i> Elvitegravir/ Cobicistat/ Emtricitabine/ Tenofovir Disoproxil Fumarate (EVG/COBI/ FTC/TDF) <i>Stribild</i>	<u>EVG Tablet (Vitekta):</u> <ul style="list-style-type: none"> • 85 mg • 150 mg 	<u>Standard Adult Dose (Vitekta):</u> <ul style="list-style-type: none"> • EVG (as Vitekta) must be used in combination with an HIV PI co-administered with RTV and another ARV drug. 	Insufficient data are available on placental transfer of EVG/COBI. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.															
	<u>Tablet (Stribild):</u> <ul style="list-style-type: none"> • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TDF 300 mg 	Recommended Elvitegravir Dosage Taken Once Daily with Food (All Drugs Administered Orally)																
Elvitegravir/ Cobicistat/ Emtricitabine/ Tenofovir Alafenamide (EVG/COBI/FTC/ TAF) <i>Genvoya</i>	<u>Tablet (Genvoya):</u> <ul style="list-style-type: none"> • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg 	<table border="1"> <thead> <tr> <th>Dosage of Elvitegravir</th> <th>Dosage of Concomitant PI</th> <th>Dosage of Concomitant RTV</th> </tr> </thead> <tbody> <tr> <td rowspan="2">85 mg once daily</td> <td>ATV 300 mg once daily</td> <td>100 mg once daily</td> </tr> <tr> <td>LPV 400 mg twice daily</td> <td>100 mg twice daily</td> </tr> <tr> <td rowspan="3">150 mg once daily</td> <td>DRV 600 mg twice daily</td> <td>100 mg twice daily</td> </tr> <tr> <td>FPV 700 mg twice daily</td> <td>100 mg twice daily</td> </tr> <tr> <td>TPV 500 mg twice daily</td> <td>200 mg twice daily</td> </tr> </tbody> </table>	Dosage of Elvitegravir	Dosage of Concomitant PI	Dosage of Concomitant RTV	85 mg once daily	ATV 300 mg once daily	100 mg once daily	LPV 400 mg twice daily	100 mg twice daily	150 mg once daily	DRV 600 mg twice daily	100 mg twice daily	FPV 700 mg twice daily	100 mg twice daily	TPV 500 mg twice daily	200 mg twice daily	
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		<u>Standard Adult Dose (Stribild and Genvoya):</u> <ul style="list-style-type: none"> • One tablet once daily with food. <u>PK in Pregnancy:</u> <ul style="list-style-type: none"> • PK studies in human pregnancy limited to case report of 1 woman. <u>Dosing in Pregnancy:</u> <ul style="list-style-type: none"> • Insufficient data to make dosing recommendation. 																

^a Individual antiretroviral drug dosages may need to be adjusted in renal or hepatic insufficiency (for details, see [Adult and Adolescent Guidelines, Appendix B, Table 7](#)).

Key to Abbreviations: ARV = antiretroviral; ATV = atazanavir; COBI = cobicistat; DRV = darunavir; EVG = elvitegravir; FPV = fosamprenavir; FTC = emtricitabine; LPV = lopinavir; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; **TAF = tenofovir alafenamide**; TDF = tenofovir disoproxil fumarate; TPV = tipranavir

References

1. Elvitegravir [package insert]. Food and Drug Administration. 2015. Available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/203093s0021b1.pdf. Accessed July 15, 2016.
2. Schalkwijk S, Colbers A, Konopnicki D, et al. First reported use of elvitegravir and cobicistat during pregnancy. *AIDS*. 2016;30(5):807-808. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26913711>.
3. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 July 2015. Wilmington, NC: Registry Coordinating Center. 2015. Available at <http://www.apregistry.com/>.