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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Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy

Table 9. Antiretroviral Drug Use in Pregnant Women with HIV: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 1 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
NRTIs NRTIs are recommended for use as part of combination regimens, usually including 2 NRTIs with either an NNRTI or 1 or more PIs. Use of single or dual NRTIs alone is not recommended for treatment of HIV infection. See text for discussion of potential maternal and infant mitochondrial toxicity.				
Abacavir (ABC) *Ziagen* (ABC/3TC) *Epzicom* (ABC/3TC/ZDV) *Trizivir* (ABC/3TC/DTG) *Triumeq*	ABC (Ziagen)[e] *Tablet:* • 300 mg *Solution:* • 20 mg/mL Epzicom:[e] • ABC 600 mg plus 3TC 300 mg tablet Trizivir:[e] • ABC 300 mg plus 3TC 150 mg plus ZDV 300 mg tablet Triumeq: • ABC 600 mg plus 3TC 300 mg plus DTG 50 mg tablet	Standard Adult Doses *ABC (Ziagen):* • 300 mg twice daily or 600 mg once daily, without regard to food *Epzicom:* • 1 tablet once daily without regard to food *Trizivir:* • 1 tablet twice daily without regard to food *Triumeq:* • 1 tablet daily without regard to food PK in Pregnancy: • PK not significantly altered in pregnancy. Dosing in Pregnancy: • No change in dose indicated.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Hypersensitivity reactions occur in approximately 5% to 8% of non-pregnant individuals; a much smaller percentage are fatal and are usually associated with re-challenge. Rate in pregnancy is unknown. Testing for HLA-B*5701 identifies patients at risk of reactions and should be done and documented as negative before starting ABC. Patients should be educated regarding symptoms of hypersensitivity reaction.	November 14, 2017
Didanosine (ddI) *Videx* *Videx EC*	ddI (Videx) *Buffered Tablets (Non-EC):* • No longer available *Solution:* • 10 mg/mL oral solution Videx EC (EC Beadlets) Capsules: • 125 mg • 200 mg • 250 mg • 400 mg Generic Delayed-Release Capsules: • 200 mg • 250 mg • 400 mg	Standard Adult Doses *Body Weight ≥60 kg:* • 400 mg once daily *With TDF:* • 250 mg once daily; take 1/2 hour before or 2 hours after a meal. *Body Weight <60kg:* • 250 mg once daily *With TDF:* • 200 mg once daily; take 1/2 hour before or 2 hours after a meal. **Note:** Preferred dosing with oral solution is twice daily (total daily dose divided into 2 doses); take 1/2 hour before or 2 hours after a meal.	Low-moderate placental transfer to fetus.[b] In the Antiretroviral Pregnancy Registry, an increased rate of birth defects with ddI compared to general population was noted after both first-trimester (20/423, 4.7%; 95% CI, 2.9% to 7.2%) and later exposure (20/461, 4.3%; 95% CI 2.7% to 6.6%). No specific pattern of defects was noted and clinical relevance is uncertain. ddI **should not be used** with d4T. Lactic acidosis, sometimes fatal, has been reported in pregnant women receiving ddI and d4T together.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 2 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
		PK in Pregnancy: • PK not significantly altered in pregnancy. Dosing in Pregnancy: • No change in dose indicated.		
Emtricitabine (FTC) *Emtriva* (FTC/TDF) *Truvada* (FTC/TDF/EFV) *Atripla* (FTC/TDF/RPV) *Complera* (FTC/TDF/EVG/COBI) *Stribild* (FTC/TAF) *Descovy* (FTC/TAF/RPV *Odefsey* (FTC/TAF/EVG/COBI) *Genvoya*	Emtriva (FTC) *Capsules:* • 200 mg *Oral Solution:* • 10 mg/mL Truvada: • FTC 200 mg plus TDF 300 mg tablet Atripla: • FTC 200 mg plus TDF 300-mg plus EFV[c] 600 mg tablet Complera: • FTC 200 mg plus TDF 300 mg plus RPV 25 mg tablet Stribild: • FTC 200 mg plus TDF 300 mg plus EVG 150 mg plus COBI 150 mg tablet Descovy: • FTC 200 mg plus TAF 25 mg tablet Odefsey: • FTC 200 mg plus TAF 25 mg plus RPV 25 mg tablet Genvoya: • FTC 200 mg plus TAF 10 mg plus EVG 150 mg plus COBI 150 mg tablet	Standard Adult Dose *Emtriva (FTC)* Capsule: • 200 mg once daily without regard to food Oral Solution: • 240 mg (24 mL) once daily without regard to food *Truvada:* • 1 tablet once daily without regard to food *Atripla:* • 1 tablet once daily at or before bedtime. Take on an empty stomach to reduce side effects. *Complera:* • 1 tablet once daily with food *Stribild:* • 1 tablet once daily with food *Descovy:* • 1 tablet once daily with or without food *Odefsey:* • 1 tablet once daily with food *Genvoya:* • 1 tablet once daily with food PK in Pregnancy: • PK of FTC not significantly altered in pregnancy. Dosing in Pregnancy: • No change in FTC dose indicated. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., TDF, TAF, EFV, RPV, EVG/c)	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). If HBV-coinfected, it is possible that a HBV flare may occur if the drug is stopped; see HIV/Hepatitis B Virus Coinfection.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 3 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Lamivudine (3TC) *Epivir* (3TC/ZDV) *Combivir* (3TC/ABC) *Epzicom* (3TC/ZDV/ABC) *Trizivir* (3TC/ABC/DTG) *Triumeq*	3TC (Epivir) *Tablets:* • 150 mg[e] • 300 mg[e] *Oral Solution:* • 10 mg/mL[e] Combivir: • 3TC 150 mg plus ZDV 300 mg tablet[e] Epzicom: • 3TC 300 mg plus ABC 600 mg tablet[e] Trizivir: • 3TC 150 mg plus ZDV 300 mg plus ABC 300 mg tablet[e] Triumeq: • 3TC 300 mg plus ABC 600 mg plus DTG 50 mg tablet	Standard Adult Dose *3TC (Epivir):* • 150 mg twice daily or 300 mg once daily, without regard to food *Combivir:* • 1 tablet twice daily without regard to food *Epzicom:* • 1 tablet once daily without regard to food *Trizivir:* • 1 tablet twice daily without regard to food *Triumeq:* • 1 tablet once daily without regard to food PK in Pregnancy: • PK not significantly altered in pregnancy. Dosing in Pregnancy: • No change in dose indicated.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). If HBV-coinfected, it is possible that an HBV flare may occur if the drug is stopped; see HIV/Hepatitis B Virus Coinfection .	November 14, 2017
Stavudine (d4T) *Zerit* **Note:** Generic products available for all formulations.	d4T (Zerit) *Capsules:* • 15 mg • 20 mg • 30 mg • 40 mg *Oral Solution:* • 1 mg/mL following reconstitution	Standard Adult Dose[f] *Body Weight ≥60 kg:* • 40 mg twice daily without regard to meals *Body Weight <60 kg:* • 30 mg twice daily without regard to meals PK in Pregnancy: • PK not significantly altered in pregnancy. Dosing in Pregnancy: • No change in dose indicated.	High placental transfer.[b] No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects). d4T **is not recommended** for pregnant women. Lactic acidosis, sometimes fatal, has been reported in pregnant women receiving ddI and d4T together.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 4 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Tenofovir Alafenamide (TAF) *Vemlidy*[d] (TAF/FTC/EVG/COBI) *Genvoya* (TAF/FTC/RPV) *Odefsey* (TAF/FTC) *Descovy*	Vemlidy • TAF 25 mg tablet Genvoya: • TAF 10 mg plus FTC 200 mg plus EVG 150 mg plus COBI 150 mg tablet Odefsey: • TAF 25 mg plus FTC 200 mg plus RPV 25 mg tablet Descovy: • TAF 25 mg plus FTC 200 mg tablet	Standard Adult Dose *Vemlidy:* • 1 tablet once daily with food *Genvoya, Odefsey:* • 1 tablet once daily with food *Descovy:* • 1 tablet once daily with or without food • Same dose (TAF 25 mg) can be used with or without pharmaco-enhancers PK in Pregnancy: • No PK studies in human pregnancy Dosing in Pregnancy: • Insufficient data to make dosing recommendation	No data are available on placental transfer of TAF. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats. Renal function should be monitored because of potential for renal toxicity.	November 14, 2017
Tenofovir Disoproxil Fumarate (TDF) *Viread* (TDF/FTC) *Truvada* (TDF/FTC/EFV) *Atripla* (TDF/FTC/RPV) *Complera* (TDF/FTC/EVG/COBI) *Stribild*	TDF (Viread) *Tablet:* • 300 mg *Powder:* • 40 mg/1 g oral powder Truvada: • TDF 300 mg plus FTC 200 mg tablet Atripla: • TDF 300 mg plus FTC 200 mg plus EFV[c] 600 mg tablet Complera: • TDF 300 mg plus FTC 200 mg plus RPV 25 mg tablet Stribild: • TDF 300 mg plus FTC 200 mg plus EVG 150 mg plus COBI 150 mg tablet	Standard Adult Dose *TDF (Viread)* *Tablet:* • 300 mg once daily without regard to food *Powder:* • 8 mg/kg (up to maximum 300 mg), take with food *Truvada:* • 1 tablet once daily without regard to food *Atripla:* • 1 tablet once daily at or before bedtime. Take on an empty stomach to reduce side effects. *Complera:* • 1 tablet once daily with food *Stribild:* • 1 tablet once daily with food PK in Pregnancy: • AUC lower in third trimester than postpartum but trough levels adequate Dosing in Pregnancy: • No change in dose indicated.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Studies in monkeys (at doses approximately 2-fold higher than that for human therapeutic use) show decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy. Human studies demonstrate no consistent link to low birth weight, but data are conflicting about potential effects on growth outcomes later in infancy. If HBV-coinfected, it is possible that an HBV flare may occur if TDF is stopped; see HIV/Hepatitis B Virus Coinfection. Renal function should be monitored because of potential for renal toxicity.	October 19, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 5 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Zidovudine (ZDV, AZT) *Retrovir* (ZDV/3TC) *Combivir* (ZDV/3TC/ABC) *Trizivir* **Note:** Generics are approved for all formulations	ZDV (Retrovir) *Capsule:* • 100 mg *Tablet:* • 300 mg *Oral Solution:* • 10 mg/mL *Intravenous Solution:* • 10 mg/mL Combivir: • ZDV 300 mg plus 3TC 150 mg tablet Trizivir: • ZDV 300 mg plus 3TC 150 mg plus ABC 300 mg tablet	Standard Adult Dose *ZDV (Retrovir):* • 300 mg BID or 200 mg TID, without regard to food *Active Labor:* • 2 mg/kg IV loading dose, followed by 1 mg/kg/hour continuous infusion from beginning of active labor until delivery *Combivir:* • 1 tablet twice daily, without regard to food *Trizivir:* • 1 tablet twice daily, without regard to food PK in Pregnancy: • PK not significantly altered in pregnancy. Dosing in Pregnancy: • No change in dose indicated.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects).	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 6 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
NNRTI NNRTIs are recommended for use in combination regimens with 2 NRTI drugs. Hypersensitivity reactions, including hepatic toxicity and rash, more common in women; unclear if increased in pregnancy.				
Efavirenz (EFV) *Sustiva* (EFV/TDF/FTC) *Atripla*	EFV (Sustiva)[e] *Capsules:* • 50 mg • 200 mg *Tablet:* • 600 mg Atripla: • EFV 600 mg plus TDF 300 mg plus FTC 200 mg tablet	Standard Adult Dose *EFV (Sustiva):* • 600 mg once daily at or before bedtime, on empty stomach to reduce side effects *Atripla:* • 1 tablet once daily at or before bedtime, on empty stomach to reduce side effects PK in Pregnancy: • AUC decreased during third trimester, compared with postpartum, but nearly all third-trimester participants exceeded target exposure. Dosing in Pregnancy: • No change in dose indicated.	Moderate placental transfer to fetus.[b] Potential fetal safety concern: The FDA advises women to avoid becoming pregnant while taking EFV and advises health care providers to avoid administration in the first trimester of pregnancy as fetal harm may occur. Although the limited data on first-trimester EFV exposure cannot rule out a 2- or 3-fold increased incidence of a rare outcome, such as neural tube defects, the available data from a meta-analysis on more than 2,000 births suggest that there is not a large increase (e.g., a 10-fold increase to a rate of 1%) in the risk of neural tube defects with first-trimester exposure. As a result, the current Perinatal Guidelines do not include a restriction of use of EFV in pregnant women or in women planning to become pregnant, consistent with both the British HIV Association and WHO guidelines for use of ARV drugs in pregnancy. EFV should be continued in pregnant women receiving a virologically suppressive EFV-based regimen, because ARV drug changes during pregnancy may be associated with loss of viral control and increased risk of perinatal transmission (see Pregnant Women Living with HIV Who are Currently Receiving Antiretroviral Therapy).	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 7 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Etravirine (ETR) *Intelence*	Tablets: • 25 mg • 100 mg • 200 mg For patients unable to swallow tablets whole, the tablets may be dispersed in a glass of water.	Standard Adult Dose(s): • 200 mg twice daily with food PK in Pregnancy: • PK data in pregnancy (n = 26) suggest 1.2–1.6-fold increased etravirine exposure during pregnancy. Dosing in Pregnancy: • No change in dose indicated.	Variable placental transfer, usually in the moderate to high categories, ranging from 0.19–4.25 (data from 19 mother-infant pairs).[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.	November 14, 2017
Nevirapine (NVP) *Viramune Viramune XR (Extended Release)* **Note:** Generic available for all formulations	NVP (Viramune) *Tablets:* • 200 mg *Oral Suspension:* • 50 mg/5 mL Viramune XR Tablets: • 100 mg • 400 mg	Standard Adult Dose: • 200 mg once daily Viramune immediate release for 14 days (lead-in period); thereafter, 200 mg twice daily or 400 mg (Viramune XR tablet) once daily, without regard to food. • Repeat lead-in period if therapy is discontinued for >7 days. • In patients who develop mild-to-moderate rash without constitutional symptoms during lead-in, continue lead-in dosing until rash resolves, but ≤28 days total. PK in Pregnancy: • PK of immediate release tablets not significantly altered in pregnancy. • No data are available on extended release (Viramune XR) formulations in pregnancy. Dosing in Pregnancy: • No change in dose indicated.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects and 2-fold increase in risk of birth defects in more common classes, cardiovascular and genitourinary). Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 cell counts ≥250/mm^3 when first initiating therapy; pregnancy does not appear to increase risk. NVP should be initiated in pregnant women with CD4 cell counts ≥250 cells/mm^3 only if benefit clearly outweighs risk because of potential increased risk of life-threatening hepatotoxicity in women with high CD4 cell counts. Elevated transaminase levels at baseline may increase the risk of NVP toxicity. Women who become pregnant while taking NVP-containing regimens and are tolerating them well can continue therapy, regardless of CD4 cell count.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 8 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Rilpivirine (RPV) *Edurant* (RPV/TDF/FTC) *Complera* (RPV/TAF/FTC) *Odefsey*	RPV (Edurant) *Tablets:* • 25 mg Complera: • RPV 25 mg plus TDF 300 mg plus FTC 200 mg tablet Odefsey: • RPV 25 mg plus TAF 25 mg plus FTC 200 mg tablet	Standard Adult Dose *RPV (Edurant):* • 25 mg once daily with food *Complera:* • 1 tablet once daily with food *Odefsey:* • 1 tablet once daily with food PK in Pregnancy: • RPV PK highly variable during pregnancy. RPV AUC and trough concentration reduced 20% to 50% in pregnancy compared with postpartum. While most pregnant women exceeded target exposure, those with detectable viral loads had lower RPV troughs. Dosing in Pregnancy: • While RPV plasma concentration is reduced during pregnancy, higher-than-standard doses have not been studied. Insufficient data are available to recommend a dosing change in pregnancy. With standard dosing, viral loads should be monitored more frequently.	Moderate to high placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects).	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 9 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
PIs PIs are recommended for use in combination regimens with 2 NRTI drugs. Hyperglycemia, new onset or exacerbation of diabetes mellitus, and diabetic ketoacidosis reported with PI use; unclear if pregnancy increases risk. Conflicting data regarding preterm delivery in women receiving PIs (see Combination Antiretroviral Drug Regimens and Pregnancy Outcomes).				
Atazanavir (ATV) *Reyataz* **Note:** Must be combined with low-dose RTV boosting in pregnancy **Atazanavir/ Cobicistat** (ATV/COBI) *Evotaz*	Atazanavir (Reyataz) *Capsules*: • 150 mg • 200 mg • 300 mg *Oral Powder:* • 50-mg packet Evotaz: • ATV 300 mg plus COBI 150 mg tablet	**Standard Adult Dose** Atazanavir (Reyataz) *ARV-Naive Patients* *Without RTV Boosting*: • ATV 400 mg once daily with food; ATV without RTV boosting **is not recommended** when used with TDF, H_2-receptor antagonists, PPIs, or during pregnancy. *With RTV Boosting*: • ATV 300 mg plus RTV 100 mg once daily with food • When combined with EFV in ARV-naive patients: ATV 400 mg plus RTV 100 mg once daily with food *ARV-Experienced Patients:* • ATV 300 mg plus RTV 100 mg once daily with food • Do not use with PPIs or EFV. • If combined with an H_2-receptor antagonist: ATV 300 mg plus RTV 100 mg once daily with food • If combined with an H_2-receptor antagonist and TDF: ATV 400 mg plus RTV 100 mg once daily with food Powder Formulation: • Oral powder is taken once daily with food at the same recommended adult dosage as the capsules along with RTV. Atazanavir/Cobicistat (Evotaz): • 1 tablet once daily with food. PK in Pregnancy *Atazanavir (Reyataz):* • ATV concentrations reduced during pregnancy; further reduced when given concomitantly with TDF or H_2-receptor antagonist. *Atazanavir/Cobicistat (Evotaz):* • No PK studies in human pregnancy.	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Must be given as low-dose RTV-boosted regimen in pregnancy. Effect of *in utero* ATV exposure on infant indirect bilirubin levels is unclear. Non-pathologic elevations of neonatal hyperbilirubinemia have been observed in some but not all clinical trials to date. Oral powder (but **not** capsules) contains phenylalanine, which can be harmful to patients with phenylketonuria.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 10 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
		Dosing in Pregnancy *Atazanavir [Reyataz]:* • Use of unboosted ATV **is not recommended** during pregnancy. • Use of ATV not recommended for treatment-experienced pregnant women taking TDF **and** an H_2-receptor antagonist. • Use of an increased dose (400 mg ATV plus 100 mg RTV once daily with food) during the second and third trimesters results in plasma concentrations equivalent to those in non-pregnant adults on standard dosing. Although some experts recommend increased ATV dosing in all women during the second and third trimesters, the package insert recommends increased ATV dosing only for ARV-experienced pregnant women in the second and third trimesters also receiving either TDF or an H_2-receptor antagonist. *Atazanavir/Cobicistat (Evotaz):* • Insufficient data to make dosing recommendation in pregnancy (see Cobicistat section).		November 14, 2017
Darunavir (DRV) *Prezista* **Note:** Must be combined with low-dose RTV or COBI boosting **Darunavir/ Cobicistat** (DRV/COBI) *Prezcobix*	DRV Tablets: • 75 mg • 150 mg • 600 mg • 800 mg DRV Oral Suspension: • 100 mg/mL Prezcobix Tablet (Co-Formulated): • DRV 800 mg plus COBI 150 mg	Standard Adult Dose *ARV-Naive Patients:* • DRV 800 mg plus RTV 100 mg once daily with food • DRV 800 mg plus COBI 150 mg once daily with food *ARV-Experienced Patients:* *If No DRV Resistance Mutations:* • DRV 800 mg plus RTV 100 mg once daily with food • DRV 800 mg plus COBI 150 mg once daily with food *If Any DRV Resistance Mutations:* • DRV 600 mg plus RTV 100 mg twice daily with food PK in Pregnancy: • Decreased exposure in pregnancy with use of DRV/r. Dosing in Pregnancy: • The Panel **does not recommend** once-daily dosing with DRV/r during pregnancy. • Twice-daily DRV/r dosing (DRV 600 mg plus RTV 100 mg with food) recommended for all pregnant women. • Increased twice-daily DRV dose (DRV 800 mg plus RTV 100 mg with food) during pregnancy does not result in an increase in darunavir exposure and **is not recommended**. • No pregnancy PK/safety data for DRV/c co-formulation, so not recommended for use in pregnancy.	Low placental transfer to fetus.[b] No evidence of teratogenicity in mice, rats, or rabbits. No evidence of human teratogenicity. Must be boosted with low-dose RTV.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 11 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Fosamprenavir (FPV) *Lexiva (a prodrug of amprenavir)* **Note:** Must be combined with low-dose RTV boosting in pregnancy	Tablets: • 700 mg Oral Suspension: • 50 mg/mL	Standard Adult Dose *ARV-Naive Patients:* • FPV 1400 mg twice daily without food, *or* • FPV 1400 mg plus RTV 100 or 200 mg once daily without food, *or* • FPV 700 mg plus RTV 100 mg twice daily without food *PI-Experienced Patients* • Once-daily dosing not recommended • FPV 700 mg plus RTV 100 mg twice daily without food *Co-Administered with EFV:* • FPV 700 mg plus RTV 100 mg twice daily without food; *or* • FPV 1400 mg plus RTV 300 mg once daily without food PK in Pregnancy: • With RTV boosting, AUC is reduced during the third trimester. However, exposure is greater during the third trimester with boosting than in non-pregnant adults without boosting, and trough concentrations achieved during the third trimester were adequate for patients without PI resistance mutations. Dosing in Pregnancy: • Use of unboosted FPV or once-daily FPV with RTV boosting **is not recommended** during pregnancy. No change is indicated in standard boosted twice-daily dose (FPV 700 mg plus RTV 100 mg twice daily without food).	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. Increased fetal loss in rabbits but no increase in defects in rats and rabbits. Must be given as low-dose RTV-boosted regimen in pregnancy.	November 14, 2017
Indinavir (IDV) *Crixivan* **Note:** Must be combined with low-dose RTV boosting in pregnancy	Capsules: • 200 mg • 400 mg	Standard Adult Dose *Without RTV Boosting:* • IDV 800 mg every 8 hours, taken 1 hour before or 2 hours after meals; may take with skim milk or low-fat meal. *With RTV Boosting:* • IDV 800 mg plus RTV 100 mg twice daily without regard to meals PK in Pregnancy: • IDV exposure markedly reduced when administered without RTV boosting during pregnancy. IDV exposure low with IDV 400 mg/RTV 100 mg dosing during pregnancy; no PK data available on alternative boosted dosing regimens in pregnancy. Dosing in Pregnancy: • Use of unboosted IDV **is not recommended** during pregnancy.	Minimal placental transfer to fetus.[b] No evidence of human teratogenicity in cases reported to the Antiretroviral Pregnancy Registry (can rule out 2-fold increase in overall birth defects). Must be given as low-dose, RTV-boosted regimen in pregnancy. Theoretical concern regarding increased indirect bilirubin levels, which may exacerbate physiologic hyperbilirubinemia in neonates. Minimal placental passage mitigates this concern.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 12 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Lopinavir/ Ritonavir (LPV/r) *Kaletra* **Note:** Generic available for some formulations	Tablets (Co-Formulated): • LPV 200 mg plus RTV 50 mg • LPV 100 mg plus RTV 25 mg Oral Solution: • LPV 400 mg plus RTV 100 mg/5 mL	Standard Adult Dose: • LPV 400 mg plus RTV 100 mg twice daily, *or* • LPV 800 mg plus RTV 200 mg once daily *Tablets:* • Take without regard to food. *Oral Solution:* • Take with food. With EFV or NVP (PI-Naive or PI-Experienced Patients): • LPV 500 mg plus RTV 125 mg tablets twice daily without regard to meals (use a combination of two LPV 200 mg plus RTV 50 mg tablets and one LPV 100 mg plus RTV 25 mg tablet), *or* • LPV 520 mg plus RTV 130 mg oral solution (6.5 mL) twice daily with food PK in Pregnancy: • With twice-daily dosing, LPV exposure is reduced in pregnant women receiving standard adult doses; increasing the dose by 50% results in exposure equivalent to that seen in non-pregnant adults receiving standard doses. • No PK data are available for once-daily dosing in pregnancy. Dosing in Pregnancy: • Once daily dosing **is not recommended** during pregnancy. • Some experts recommend that an increased dose (i.e., LPV 600 mg plus RTV 150 mg twice daily without regard to meals or LPV 500 mg plus RTV 125 mg twice daily without regard to meals) should be used in the second and third trimesters, especially in PI-experienced pregnant women and women who start treatment during pregnancy with a baseline viral load >50 copies/mL. • If standard dosing is used, monitor virologic response and LPV drug levels, if available..	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Oral solution contains 42% alcohol and 15% propylene glycol and is not recommended for use in pregnancy. Once-daily LPV/r dosing is not recommended during pregnancy	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 13 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Nelfinavir (NFV) *Viracept*	Tablets: • 250 mg • 625 mg (tablets can be dissolved in small amount of water) Powder for Oral Suspension: • 50 mg/g	Standard Adult Dose: • 1250 mg twice daily or 750 mg three times daily with food PK in Pregnancy: • Lower NFV exposure in third trimester than postpartum in women receiving NFV 1250 mg twice daily; however, generally adequate drug levels are achieved during pregnancy, although levels are variable in late pregnancy. Dosing in Pregnancy: • Three-times-daily dosing with 750 mg with food not recommended during pregnancy. No change in standard dose (1250 mg twice daily with food) indicated.	Minimal to low placental transfer to fetus.[b] No evidence of human teratogenicity; can rule out 1.5-fold increase in overall birth defects and 2-fold increase in risk of birth defects in more common classes, cardiovascular, and genitourinary. Contains aspartame; should not be used in individuals with phenylketonuria.	November 14, 2017
Saquinavir (SQV) *Invirase* **Note:** Must be combined with low-dose RTV for PK boosting	Tablet: • 500 mg Capsule: • 200 mg	Standard Adult Dose: • SQV 1000 mg plus RTV 100 mg twice a day with food or within 2 hours after a meal PK in Pregnancy: • Based on limited data, SQV exposure may be reduced in pregnancy but not sufficient to warrant a dose change. Dosing in Pregnancy: • No change in dose indicated.	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. Must be boosted with low-dose RTV. Baseline ECG recommended before starting because PR and/or QT interval prolongations have been observed. Contraindicated in patients with preexisting cardiac conduction system disease.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 14 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Tipranavir (TPV) *Aptivus* **Note:** Must be combined with RTV for PK boosting	Capsules: • 250 mg Oral Solution: • 100 mg/mL	Standard Adult Dose: • TPV 500 mg plus RTV 200 mg twice daily *With RTV Tablets:* • Take with food. *With RTV Capsules or Solution:* • Take without regard to food; however, administering with food may help make the dose more tolerable. PK in Pregnancy: • Limited PK data in human pregnancy Dosing in Pregnancy: • Insufficient data to make dosing recommendation	Moderate placental transfer to fetus reported in 1 patient.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. Must be given as low-dose RTV-boosted regimen.	November 14, 2017
Entry Inhibitors				
Enfuvirtide (T-20) *Fuzeon*	Injectable: • Supplied as lyophilized powder. Each vial contains 108 mg of T-20; reconstitute with 1.1 mL of sterile water for injection for SQ delivery of approximately 90 mg/1 mL.	T-20 is indicated for advanced HIV disease and must be used in combination with other ARV drugs to which the patient's virus is susceptible by resistance testing. Standard Adult Dose: • 90 mg (1 mL) twice daily without regard to meals PK in Pregnancy: • No PK data in human pregnancy. Dosing in Pregnancy: • Insufficient data to make dosing recommendation.	Minimal to low placental transfer to fetus.[b] No data on human teratogenicity.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 15 of 19)

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**	**Use in Pregnancy**	**Last Reviewed**
Maraviroc (MVC) *Selzentry*	Tablets: • 150 mg • 300 mg	Standard Adult Dose: • 300 mg twice daily with or without food • Maraviroc should only be used for patients with CCR5-tropic virus (and no X4-tropic virus). Dose Adjustments: • Increase to 600 mg BID when used with potent CYP3A inducers: EFV, ETR, and rifampin. • Decrease to 150 mg BID when used with CYP3A inhibitors: all PIs except TPV/r, itraconazole. PK in Pregnancy: • A PK study in human pregnancy demonstrated a 20% to 30% overall decrease in AUC, but C_{trough} exceeded the recommended minimal concentration of 50 ng/mL. Dosing in Pregnancy: • Standard adult dosing adjusted for concomitant ARV use appears appropriate.	No evidence of teratogenicity in rats or rabbits; insufficient data to assess for teratogenicity in humans. MVC placental passage category should be moderate.[b]	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 16 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Integrase Inhibitors				
Dolutegravir (DTG) *Tivicay* (DTG/ABC/3TC) *Triumeq*	DTG Tablets: • 50 mg Triumeq: • DTG 50 mg plus ABC 600 mg plus 3TC 300 mg tablet	Standard Adult Dose *ARV-Naive or ARV-Experienced (but Integrase Inhibitor-Naive Patients)* *DTG (Tivicay):* • 1 tablet once daily, without regard to food. *DTG/ABC/3TC (Triumeq):* • 1 tablet once daily, without regard to food. *ARV-Naive or ARV-Experienced (but Integrase Inhibitor-Naive) if Given with EFV, FPV/r, TPV/r, or Rifampin; or Integrase Inhibitor-Experienced* *DTG (Tivicay):* • 1 tablet twice daily, without regard to food. PK in Pregnancy: • AUC may be decreased during the third trimester compared with postpartum, but good viral suppression in third trimester recipients. Dosing in Pregnancy: • No change in dose indicated.	High placental transfer to fetus. No evidence of teratogenicity in mice, rats, or rabbits. Preliminary data suggest no increased risk of teratogenicity in humans.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 17 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Elvitegravir (EVG) *Vitekta* **Note:** As of October 2017, Vitekta (i.e., EVG as a single-entity formulation) is no longer available **Elvitegravir/ Cobicistat/ Emtricitabine/ Tenofovir Disoproxil Fumarate** (EVG/COBI/ FTC/TDF) *Stribild* **Elvitegravir/ Cobicistat/ Emtricitabine/ Tenofovir Alafenamide** (EVG/COBI/FTC/TAF) *Genvoya*	Tablet (Stribild): • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TDF 300 mg Tablet (Genvoya): • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg	Standard Adult Dose (Stribild and Genvoya): • 1 tablet once daily with food. PK in Pregnancy: • PK studies in women who received EVG/c demonstrated significant reduction in EVG plasma exposure during pregnancy. Dosing in Pregnancy: • Insufficient data to make dosing recommendation.	Evidence of high placental transfer of EVG and low transfer of COBI. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. EVG/c **is not recommended** for initial use in pregnancy. For women who become pregnant while taking EVG/c, consider switching to a more effective, recommended regimen. If an EVG/c regimen is continued, viral load should be monitored frequently, and TDM (if available) may be useful.	November 14, 2017
Raltegravir (RAL) *Isentress* *Isentress HD*	Isentress *Film-Coated Tablets:* • 400 mg *Chewable Tablets:* • 25 mg • 100 mg Isentress HD *Film-Coated Tablets:* • 600 mg	Standard Adult Dose: • 400-mg film-coated tablets twice daily without regard to food. • Two, 600-mg film-coated (1200 mg) once daily for treatment-naive patients or patients already virologically suppressed on initial regimen of RAL 400 mg BID) without regard to food • Chewable and oral suspension doses are not interchangeable to either film-coated tablets or to each other. *With Rifampin:* • Two, 400-mg film-coated tablets (800 mg) twice daily without regard to food. PK in Pregnancy: • Decreased levels in third trimester not of sufficient magnitude to warrant change in dosing. Dosing in Pregnancy: • No change in dose indicated. • Once-daily dosing (i.e., two 600-mg film-coated tablets) should not be used in pregnant women until more information is available.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Case report of markedly elevated liver transaminases with use in late pregnancy. Severe, potentially life-threatening and fatal skin and hypersensitivity reactions have been reported in non-pregnant adults. Chewable tablets contain phenylalanine.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 18 of 19)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Pharmaco-Enhancers				
Cobicistat (COBI) *Tybost* **Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine** (EVG/COBI/ TDF/FTC) *Stribild* **Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine** (EVG/COBI/TAF/FTC) *Genvoya* **Atazanavir/Cobicistat** (ATV/COBI) *Evotaz* **Darunavir/Cobicistat** (DRV/COBI) *Prezcobix*	Tablet (Tybost): • 150 mg Tablet (Stribild): • EVG 150 mg plus COBI 150 mg plus TDF 300 mg plus FTC 200 mg Tablet (Genvoya): • EVG 150 mg plus COBI 150 mg plus TAF 10 mg plus FTC 200 mg Tablet (Evotaz): • ATV 300 mg plus COBI 150 mg Tablet (Prezcobix): • DRV 800 mg plus COBI 150 mg	Standard Adult Dose *Tybost:* • As an alternative PK booster with ATV or DRV/r: 1 tablet (150 mg) once daily with food. *Stribild, Genvoya, Evotaz, Prezcobix:* • 1 tablet once daily with food. PK in Pregnancy: • Based on limited data, COBI exposure and pharmaco-enhancing effect are markedly reduced in pregnancy. Dosing in Pregnancy: • While COBI exposure is markedly reduced during pregnancy, higher than standard doses have not been studied. The Panel recommends the use of RTV as the preferred pharmaco-enhancer during pregnancy until more data are available on COBI activity during pregnancy.	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.	November 14, 2017
Ritonavir (RTV) *Norvir*	Capsules: • 100 mg Tablets: • 100 mg Oral Solution: • 80 mg/mL Powder: • 100 mg/sachet	Standard Adult Dose as PK Booster for Other PIs: • 100–400 mg per day in 1–2 divided doses (refer to other PIs for specific dosing recommendations.) *Tablet:* • Take with food. *Capsule or Oral Solution:* • To improve tolerability, recommended to take with food if possible. PK in Pregnancy: • Lower levels during pregnancy compared with postpartum. Dosing in Pregnancy: No dosage adjustment necessary when used as booster.	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Should only be used as low-dose booster for other PIs. Oral solution contains 43% alcohol and is therefore not recommended during pregnancy, because there is no known safe level of alcohol exposure during pregnancy.	November 14, 2017

Table 9. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 19 of 19)

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

[b] Placental transfer categories—Mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6

Moderate: 0.3–0.6

Low: <0.3

[c] See Teratogenicity for discussion of EFV and risks in pregnancy.

[d] Only indicated for use in chronic HBV virus infection in adults.

[e] Generic formulation available

[f] WHO recommends maximum dose of 30 mg twice daily regardless of weight.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; AUC = area under the curve; AZT = zidovudine; BID = twice daily; CD4 = CD4 T lymphocyte; CI = confidence interval; CNS = central nervous system; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EC = enteric coated; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FPC = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HBV = hepatitis B virus; IDV = indinavir; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TID = three times a day; TPV = tipranavir; TPV/r = tipranavir/ritonavir; WHO = World Health Organization; ZDV = zidovudine