Table 30. Preclinical and Clinical Data Concerning the Use of Antiretrovirals During Pregnancy

(see **Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy** for more detail on drugs)

Antiretroviral drug	FDA pregnancy category *	Placental passage (newborn: mother drug ratio)	Long-term animal carcinogenicity studies	Animal teratogen studies
Nucleoside and nucleotide analogue reverse transcriptase inhibitors				
Abacavir (Ziagen, ABC)	C	Yes (rats)	Not completed	Positive (rodent anasarca and skeletal malformations at 1000 mg/kg (35x human exposure) during organogenesis; not seen in rabbits)
Didanosine (Videx, ddI)	B	Yes (human) [0.5]	Negative (no tumors, lifetime rodent study)	Negative
Emtricitabine (Emtriva, FTC)	B	Unkown	Not completed	Negative
Lamivudine (Epivir, 3TC)	C	Yes (human) [~1.0]	Negative (no tumors, lifetime rodent study)	Negative
Stavudine (Zerit, d4T)	C	Yes (rhesus monkey) [0.76]	Not completed	Negative (but sternal bone calcium decreases in rodents)
Tenofovir DF (Viread)	B	Yes (rat and monkey)	Not completed	Negative (osteomalacia when given to juvenile animals at high doses)
Zalcitabine (HIVID, ddC)	C	Yes (rhesus monkey) [0.30–0.50]	Positive (rodent, thymic lymphomas)	Positive (rodent-hydrocephalus at high dose)
Zidovudine† (Retrovir, AZT, ZDV)	C	Yes (human) [0.85]	Positive (rodent, noninvasive vaginal epithelial tumors)	Positive (rodent-near lethal dose)
Non-nucleoside reverse transcriptase inhibitors				
Efavirenz (Sustiva)	C	Yes (cynomologus monkey, rat, rabbit) [~1.0]	Not completed	Positive (cynomologus monkey- anencephaly, anophthalmia, microophthalmia)
Delavirdine (Rescriptor)	C	Unknown	Not completed	Positive (rodent-ventricular septal defect)
Nevirapine (Viramune)	C	Yes (human) [~1.0]	Not completed	Negative
Protease inhibitors				
Amprenavir (Agenerase)	C	Unknown	Not completed	Negative (but deficient ossification and thymic elongation in rats and rabbits)
Atazanavir (Reyataz)	B	Unknown	Not completed	Negative
Fosamprenavir (Lexiva)	C	Unknown	Positive (increased benign and malignant liver tumors in male rodents)	Negative (deficient ossification with amprenavir but not fosamprenavir)
Indinavir (Crixivan)	C	Minimal (humans)	Not completed	Negative (but extra ribs in rodents)
Lopinavir/Ritonavir (Kaletra)	C	Unknown	Not completed	Negative (but delayed skeletal ossification and increase in skeletal variations in rats at maternally toxic doses)
Nelfinavir (Viracept)	B	Minimal (humans)	Not completed	Negative
Ritonavir (Norvir)	B	Minimal (humans)	Positive (rodent, liver tumors)	Negative (but cryptorchidism in rodents)‡
Saquinavir (Fortovase)	B	Minimal (humans)	Not completed	Negative
Fusion inhibitors				
Enfuvirtide (Fuzeon)	B	Unknown	Incomplete	Negative

* Food and Drug Administration Pregnancy Categories:
A - Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and no evidence exists of risk during later trimesters).
B -Animal reproduction studies fail to demonstrate a risk to the fetus, and adequate but well-controlled studies of pregnant women have not been conducted.
C -Safety in human pregnancy has not been determined; animal studies are either positive for fetal risk or have not been conducted, and the drug should not be used unless the potential benefit outweighs the potential risk to the fetus.
D - Positive evidence of human fetal risk that is based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug among pregnant women might be acceptable despite its potential risks.
X - Studies among animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.

† Despite certain animal data indicating potential teratogenicity of zidovudine when near-lethal doses are given to pregnant rodents, substantial human data are available indicating that the risk to the fetus, if any, is limited when administered to the pregnant mother beyond 14 weeks gestation. Follow-up for ≤6 years for 734 infants who had been born to HIV-infected women and had in utero exposure to zidovudine has not demonstrated any tumor development (**Source:** Hart CE, Lennox JL, Pratt-Palmore M, et al. Correlation of HIV type 1 RNA levels in blood and the female genital tract. *J Infect Dis* 1999; 179:871-82). However, no data are available regarding longer follow-up for late effects.

‡ These effects occurred only at maternally toxic doses.