Published in final edited form as:

Curr HIV/AIDS Rep. 2024 February ; 21(1): 1–10. doi:10.1007/s11904-024-00688-y.

Antiretroviral Therapy in Pregnancy: A 2023 Review of the Literature

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Abstract

Purpose of Review—Selection of antiretroviral therapy during pregnancy must consider maternal physiology and resulting pharmacokinetic changes in pregnancy, resistance and efficacy profiles, tolerability and frequency of adverse effects, teratogenicity, and maternal, neonatal, and pregnancy outcomes. The objective of this review is to summarize the underlying data that informs the current clinical perinatal guidelines in the USA.

Recent Findings—Data now supports the use of dolutegravir at all stages of pregnancy with no significant increase in neural tube defects. Safety and pharmacokinetic data on newer antiretroviral medications in pregnancy continue to lag behind the general population.

Summary—While there are multiple safety and tolerability concerns with older regimens, there are now multiple options of regimens that are highly efficacious and have good safety data in pregnancy. Most pregnant patients who are virally suppressed on a well-tolerated regimen are able to safely continue those medications during pregnancy.

Keywords

Pregnancy; Antiretroviral therapy; Teratogenicity

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Author Contributions All authors wrote and edited the main manuscript text. All authors reviewed the manuscript

Declarations

Competing Interests The authors declare no competing interests.

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Introduction

Recent data demonstrate that women account for 18% and 22% of new and total human immunodeficiency virus (HIV) diagnoses respectively in the USA and 46% of new and 53% of total diagnoses worldwide [1, 2]. Women within reproductive age categories account for the vast majority of new infections [1, 2]. Please note that while gender-inclusive language will be used throughout this paper wherever possible, descriptions of primary data will utilize language from the original publication or data source. About 5000 people with HIV in the USA and 1.2 million worldwide give birth every year in the USA [2, 3]. While efforts to prevent initial HIV infection in persons of reproductive age are important in preventing perinatal transmission, equally important are efforts to ensure that people with HIV receive appropriate treatment. While not all reproductive-age people are interested in trying to conceive, healthcare providers must prioritize discussing reproductive goals with patients and consider these desires in the choice of antiretroviral (ARV) therapy. The Perinatal HIV Clinical Guidelines, written by the US Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission, assess the available evidence and outline evidence-based recommendations for ARV therapy during the pre-conception, pregnancy, and postpartum periods [4]. Development of guidelines for ARV in pregnancy includes consideration of pharmacokinetics in pregnancy, efficacy, simplicity and tolerability of regimens, drug-drug interactions, teratogenicity, and maternal and neonatal safety data. The purpose of this article is not to summarize existing clinical recommendations but instead to briefly review the primary data that inform clinical guidelines for the use of ARV in pregnancy.

Nucleoside Reverse Transcriptase Inhibitors

Nucleoside reverse transcriptase inhibitors (NRTIs) are the backbone of HIV treatment and prevention, both in pregnancy and in the general population. Zidovudine, a NRTI, was the first medication made available for HIV treatment in 1987 [5]. NRTIs work by inhibiting the reverse transcriptase enzyme, effectively preventing replication of the virus [6, 7]. Despite renal excretion of NRTIs and changes in renal physiology during pregnancy, studies have shown that the pharmacokinetic profiles of NRTIs do not significantly change during pregnancy [8, 9]. There are some data suggesting that genetic differences could affect NRTI levels in pregnancy, but evidence does not currently support the need for dose adjustment [10].

NRTIs are not metabolized through the CYP 450 system; therefore, fewer drug-drug interactions exist compared to non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). There are certain tuberculosis medications (including rifampin) and antiepileptic drugs (carbamazepine) however that can affect levels of certain NRTIs, so checking drug-drug interactions prior to coadministration of these drugs is recommended [11].

Some NRTI resistance mutations, with M184V being one of the most common, confer resistance to zidovudine and stavudine, and these mutations can potentially induce cross-resistance with newer NRTIs, such as abacavir and tenofovir [12]. Estimates vary for

NRTI resistance in the pregnant and postpartum population, with one study from Cameroon showing NRTI resistance during breastfeeding to be approximately 15% [13]. Resistance, especially to older NRTIs, should be considered when starting ARV medication.

Currently, no significant increase in birth defects has been noted with first-trimester exposure to regimens containing NRTIs by the Antiretroviral Pregnancy Registry. Data are sufficient to rule out a twofold increase in birth defects for didanosine, stavudine, tenofovir alafenamide, and a 1.5-fold increase for abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, and zidovudine [14••].

Historically, an association was noted between NRTI-containing regimens and poor obstetric outcomes [8]; however, current research shows conflicting results with most studies showing no significant association between prenatal exposure to NRTIs and risk of spontaneous abortion, small for gestational age, or prematurity. Some increased risk of low birth weight is seen in patients exposed to NRTI alone, but this regimen is no longer the standard of care [8, 9, 15, 16]. In general, tenofovir disoproxil fumarate/emtricitabine may be associated with larger neonates, fewer neonates that are small for gestational age, and less placental oxidative stress when compared to abacavir/lamivudine or zidovudine/lamivudine, but again, data are mixed [17, 18]. The mechanism of the adverse effects of NRTIs is thought to be through mitochondrial toxicity and oxidative stress, but the exact effect of NRTIs on the long-term health of the fetus and neonate needs more investigation [17, 19].

In terms of potential adverse effects on the pregnant person, tenofovir alafenamide has fewer renal effects than tenofovir disoproxil in the general population, and this trend is also seen in a pregnant cohort with lower creatinine at delivery for patients on tenofovir alafenamide–containing regimens as compared to efavirenz, emtricitabine, and tenofovir disoproxil fumarate containing regimens [8]. Other adverse effects such as myopathy, peripheral neuropathy, and lactic acidosis with hepatic steatosis are more common with use of zidovudine, lamivudine, stavudine, and didanosine, leading to current preference for regimens containing tenofovir/emtricitabine [7].

In summary, NRTIs, especially newer medications, are the backbone of HIV treatment in pregnancy and are generally well tolerated by both mothers and fetuses.

Non-nucleoside Reverse Transcriptase Inhibitors

NNRTIs noncompetitively inhibit reverse transcriptase by altering the binding of the enzyme to DNA [20]. NNRTIs have high oral bioavailability and undergo primarily hepatic metabolism via the cytochrome P450 (CYP 450) system, most commonly by CYP 2C and 3A enzyme families [21–24]. Because the enzymatic activity of the CYP 450 system is altered during pregnancy, plasma levels of NNRTIs differ among pregnant and non-pregnant patients. Plasma concentrations of efavirenz and rilpivirine decrease during pregnancy, while concentrations of nevirapine remain unchanged [25–27] and concentrations of etravirine increase [28]. There is insufficient data to draw conclusions about the pharmacokinetics of doravirine during pregnancy. Despite the change in plasma levels, dose adjustment is not currently recommended in pregnant patients [21, 24, 25, 29], although more frequent

monitoring of HIV viral load may be beneficial for pregnant patients on ARV regimens containing efavirenz, nevirapine, and rilpivirine due to the potential decrease. Data regarding the pharmacokinetics of injectable rilpivirine (in combination with cabotegravir) is based on a few case reports only; preliminary data suggest that plasma and washout concentrations may be similar in pregnant and non-pregnant people [30]. Because of metabolism via the CYP 450 system, there are also drug-drug interactions including with multiple medications that are commonly used in pregnancy: mood medications, including selective serotonin reuptake inhibitors (SSRIs), and certain antimicrobials, including metronidazole and fluconazole [31]. While these medications are not contraindicated, awareness of changing drug levels (both of ARV and the co-administered medication) is important.

NNRTIs have high rates of placental transfer and effectively prevent vertical transmission of HIV [21, 29, 32]. However, they are generally reserved for second- or third-line treatment due to their high susceptibility to drug resistance, as well as decreased efficacy compared to other ARV classes [21, 33]. The prevalence of HIV drug resistance to NNRTIs has been estimated to be as high as 11–15%, occurring more frequently than both NRTIs and protease inhibitors (PIs) [22, 34, 35]. The first-generation NNRTIs, nevirapine and efavirenz, have a very low threshold for resistance, and cross-resistance between these drugs is common. The second-generation NNRTIs, etravirine, rilpivirine, and doravirine have a higher threshold for resistance [22]. Previous studies have shown that several HIV strains resistant to first-generation NNRTIs are still susceptible to a second-generation formulation [21, 23, 24, 36, 37]. In terms of efficacy, regimens containing NNRTIs have been shown to be less effective in suppressing viral load at delivery than dolutegravir, an integrase strand transfer inhibitor (INSTI) [8, 38], although the rates of perinatal HIV transmission do not differ [32].

Historically, there has been concern that NNRTIs may be associated with fetal anomalies. Recent studies have shown no consistent significant association between exposure to nevirapine or rilpivirine and incidence of birth defects, although existing data are inconclusive regarding the effect of efavirenz on neural tube defects specifically or the effects of etravirine or doravirine on any birth defect [24, 29, 39, 40]. Efavirenz has been associated with microcephaly and neurodevelopmental delay in some neonates [39, 41–43]. The presence of conflicting results is one reason that efavirenz is classified as an alternative medication for initiation during pregnancy.

There are conflicting data regarding the association between in utero exposure to NNRTIs and adverse fetal and infant outcomes. Some studies have found that low birthweight may be more common among infants exposed to NNRTIs than those exposed to PIs or INSTIs, although the differences were not statistically significant [16, 44]. When compared with dolutegravir-containing regimens, efavirenz- and nevirapine-containing regimens have been shown to have a significantly higher risk of neonatal mortality [8, 39]. Nevirapine-containing regimens in particular have been associated with an increased risk of adverse birth outcomes (stillbirth, preterm delivery, low birth weight), even when compared with ARV regimens containing other NNRTIs [39, 45–47]. Data are contradictory when directly comparing NNRTIs to PI-based regimens with some studies showing increased and some studies showing decreased incidence of poor perinatal outcomes [16, 48, 49•]. There are

currently insufficient data to establish fetal and infant safety for etravirine, rilpivirine, and doravirine [21, 24, 29].

In terms of obstetric outcomes, NNRTI-based regimens have been associated with an increased risk of gestational diabetes compared to NRTI-based regimens [50]. Nevirapine-based regimens may additionally be associated with an increased risk of hypertensive disorders of pregnancy compared to regimens containing ARV from other classes [37, 39]. Pregnant patients on efavirenz-based regimens have been found to have lower total weight gain than pregnant patients on dolutegravir-based regimens [8, 39]. However, no difference in total weight gain has been found between other regimens containing NNRTIs, INSTIs, or PIs [44].

Pregnancy may increase the risk of adverse events among patients on NNRTI-based ARV regimens. Two of the most common severe adverse effects associated with NNRTIs are hepatic toxicity and skin rash, both of which may occur more frequently in pregnant patients [51]. While hepatotoxicity is theoretically possible with all NNRTIs, it seems to be primarily a concern with first-generation NNRTIs (nevirapine and efavirenz) [52]. Because there is an overlap between the symptoms of pregnancy and early hepatic toxicity, including nausea and vomiting, pregnant patients who continue NNRTI-containing ARV regimens should be monitored closely for hepatotoxicity. Efavirenz has additionally been shown to be associated with an increased risk of neuropsychiatric side effects, including insomnia, depression, and encephalopathy, especially in patients with other psychiatric conditions [39, 53, 54]. In light of these findings, mood should be monitored in pregnant patients on efavirenz-containing regimens, especially in those at increased risk for postpartum depression.

In summary, NNRTIs are not recommended as first-line therapy in pregnant patients due to the high prevalence of drug resistance, possible association with adverse birth outcomes, and insufficient data on fetal and maternal safety.

Protease Inhibitors

Protease inhibitors (PIs) as a class were first introduced in 1995 and have long been used in combination therapies with NRTIs to treat HIV. After their initial introduction, the use of PIs was particularly popular during pregnancy due to concerns that efavirenz, an NNRTI, was linked with an increased risk of neural tube defects, an association that has not been borne out in further studies [39, 55]. However, their use has since fallen out of favor, especially in high-resource settings, due to increasing associations with preterm birth and small-for-gestational-age infants, though they are often still used in low-resource areas [56•].

Pharmacokinetic studies of PIs have shown variable intracellular and plasma drug concentrations in the third trimester of pregnancy relative to the non-pregnant person. These alterations in drug concentration are largely attributable to physiologic and metabolic changes of pregnancy, although some evidence also suggests that genetic alterations affecting CYP 450 3A4 metabolism may be responsible for some reduction in bioavailability [55, 57]. Outside of pregnancy, cobicistat is used to boost the antiretroviral effects of atazanavir and darunavir; however, multiple pharmacokinetic studies showing markedly

reduced concentrations of the drug limit its use during pregnancy [58–60]. Because of these observed changes in pregnancy, the preferred PIs are administered with ritonavir, another PI, to boost third-trimester bioavailability. Dosing adjustments are recommended for darunavir and lopinavir, while atazanavir requires only once-daily dosing [61–63]. Drug interactions are extremely common between PIs and multiple classes of medications, including many that are commonly used in pregnancy such as H2-antagonists, proton-pump inhibitors, macrolide antibiotics, anti-epileptics, anti-depressants, anti-psychotics, and corticosteroids.

Challenges with drug resistance plague PIs as with many other antiretroviral drug classes. A 2022 study of PI resistance found that up to a third of patients failing second-line PI therapy had significant resistance mutations [64]. However, available data looking at the development of resistance in pregnancy suggests no significant increase in the development of PI resistance with short-term use during gestation [64, 65].

Regarding virologic efficacy, studies have demonstrated similar viral suppression and tolerability between PI-based regimens but have suggested decreased viral suppression with lopinavir compared to NNRTIs. Despite differences in viral suppression, rates of perinatal HIV transmission have not been found to differ [66, 67].

Studies of drug concentrations within cord blood have shown low transplacental passage of PIs (likely related to large molecular size and high degree of protein binding), contributing to the low risk of teratogenicity observed with this medication class [39, 55]. Concerning adverse pregnancy outcomes, the most pressing concern is the association between PI use, preterm birth, and small-for-gestational-age infants. Evidence both in vitro and in vivo suggests that PIs broadly affect progesterone, human chorionic gonadotropin, sex-hormone binding globulin, prolactin, and estrogen concentrations in pregnancy, effects which are postulated to contribute mechanistically to increased rates of preterm birth and small for gestational age infants [56•]. Meta-analyses including one published in 2023 have upheld these associations [49•, 68•, 69]. Additionally, evidence from animal models suggests that PI exposure in early pregnancy can also result in dysregulation of angiogenesis within the placenta and alterations in spiral artery remodeling and decidualization, which may contribute to the development of intrauterine growth restriction, preterm birth, or early onset severe preeclampsia [56•]. Many of these studies have been carried out using lopinavir, with less evidence existing for atazanavir or darunavir. When examining other adverse perinatal effects of PIs, a systematic review performed in 2019 found three studies that supported a correlation between PI use and hypertensive diseases of pregnancy [70].

Though generally well tolerated, side effects of PI use (both during and outside of pregnancy) include an increased risk of gastrointestinal upset with diarrhea, nausea, vomiting, and abdominal pain. Clinicians should monitor for such side effects after initiation of PIs although it may be difficult to determine which are side effects of medication versus attributable to pregnancy itself. Atazanavir carries an increased risk of maternal hyperbilirubinemia which could potentially lead to an increased risk of hyperbilirubinemia in the neonate [61].

In summary, due to possible association with adverse pregnancy outcomes (specifically preterm birth and small for gestational age infants), as well as significant drug interactions and the need for alteration in dosing in pregnancy, PIs are less often recommended as first-line therapy in high-resource settings where other regimens are available.

Entry and Attachment Inhibitors

Entry and attachment inhibitors target the HIV-1 entry process. There are several advantages to targeting the entry process: [1] The virus is blocked before integration of the viral genome into the host cell genome; [2] there is no requirement to enter cells, unlike NRTIs, NNRTIs, INSTIs, and PIs; and [3] given that the entry process comprises multiple distinct steps, there are multiple potential targets for entry inhibitors [71]. The main drugs in this class include fostemsavir, maraviroc, and ibalizumab, and they are used to treat patients with multidrug-resistant infections.

Fostemsavir is a prodrug of the active drug temsavir, which is a gp120-directed attachment inhibitor. No pharmacokinetic studies in human pregnancy have been performed on fostemsavir. There are no human data available regarding the placental passage of fostemsavir, though a study in rats demonstrated placental passage of temsavir [72]. Regarding teratogenicity, there is no data available in humans, but no evidence of teratogenicity in rat or rabbit studies at doses comparable to those used in humans [72]. Given limitations in available data, fostemsavir is not a recommended ARV agent in pregnancy, although it can be used in cases of multidrug resistant HIV in which other options are limited.

Maraviroc is a small molecule drug that inhibits the binding of HIV-1 to a co-receptor, cysteine-cysteine chemokine receptor 5 (CCR5), to prevent attachment and entry into the cell [73]. One study measured the pharmacokinetic profiles in the third trimester and postpartum in 18 individuals taking maraviroc. They concluded that standard adult dosing adjusting for concomitant ARV drugs is appropriate in pregnancy. The same study measured median cord blood-to-maternal delivery plasma drug ratios and found moderate placental transfer of maraviroc to the fetus [74]. Data in humans are insufficient to assess for potential teratogenicity of maraviroc. There is no evidence of teratogenicity in studies of rats or rabbits at dosages comparable to those used in humans [75]. Notably, a retrospective study of 857 pregnant people showed increased maternal hepatotoxicity among the 492 individuals starting ARV regimens including maraviroc in pregnancy; the adjusted hazard ratio for hepatotoxicity with maraviroc was 4.19 (95% confidence interval 1.34–13.1, $p = 0.01$) [76]. In light of limited available data, maraviroc is not recommended for use in pregnancy.

Ibalizumab is a recombinant humanized monoclonal antibody. It has a novel mechanism of action as a cluster of differentiation 4 (CD4)-directed post-attachment inhibitor, and its pharmacokinetic profile allows for dosing every 14 days after the initial loading dose [77]. There are no pharmacokinetic studies on ibalizumab in human pregnancy. No human data are available, but in general, placenta transfer of monoclonal antibodies does occur, so transfer of ibalizumab is possible [78]. Based on data collected in monkeys, there is potential for reversible immunosuppression (specifically CD4 T cell and B cell lymphocytopenia)

in infants born to people taking ibalizumab during pregnancy, similar to that seen with use of other monoclonal antibodies during pregnancy. There are no data regarding the teratogenicity of ibalizumab in humans, though a study in monkeys did not report any malformations or premature births [78]. Given insufficient available data in humans, ibalizumab is not a recommended ARV agent in pregnancy.

Overall, for these ARV medications targeting the HIV-1 entry process, there is limited data in pregnancy, and consequently, no members of these newer drug classes are currently recommended in pregnancy.

Integrase Strand Transfer Inhibitors

Integrase strand transfer inhibitors (INSTIs) were first approved for the treatment of HIV in 2007. The class, which includes raltegravir, elvitegravir, dolutegravir, bictegravir, and cabotegravir, has become common in first-line ARV regimens [79]. Notably, the World Health Organization (WHO) has recommended dolutegravir as first-line ARV for all people with HIV, including those who are pregnant or breastfeeding [80]. INSTIs prevent viral integration by blocking the integrase enzyme active site and preventing target cell infection [81]. Pharmacokinetic studies have found that physiologic changes during pregnancy decrease levels of INSTIs during the second and third trimesters [82]. For example, elvitegravir trough levels have been found to be decreased in most pregnant people, which could lead to suboptimal viral suppression, and therefore, it is not recommended for use in pregnancy [83]. Raltegravir is recommended to have twice daily dosing during pregnancy due to decreased plasma levels, while standard dosing of dolutegravir has shown appropriate target levels [84–87]. Bictegravir is a newer INSTI and is only available in a fixed-dose formulation; although data are limited, preliminary results suggest adequate levels in pregnancy [88, 89]. Due to the limited data, it is considered an alternative regimen for ARV-naïve patients during pregnancy and should be continued for people already well suppressed prior to pregnancy.

INSTIs have fewer drug-drug interactions than other classes of ARV. However, interactions with several commonly used drugs should be considered before prescribing. These include metformin, rifampin, St. John’s Wort, and various antacids [85, 90]. It is important to counsel regarding the separation of the prenatal vitamin and any antacids containing cations by at least 2 h before or 6 h after taking ARV-containing INSTIs. Lack of separation of prenatal vitamin and ARV is a common reason for viral blips in a patient with otherwise well-controlled HIV and excellent adherence during pregnancy [90].

As with other ARV classes, INSTIs have documented resistance. However, they are known for having a higher resistance barrier as compared to other ARV medications, such as NRTIs and NNRTIs [81]. First-generation drugs, such as raltegravir and elvitegravir, have several known resistance-conferring mutations and demonstrate cross-resistance [86]. Dolutegravir and bictegravir have been shown to have a greater resistance barrier than first-generation options and remain effective against HIV-1 strains that are resistant to raltegravir and elvitegravir [81]. While pharmacokinetic variations and decreased INSTI levels could

theoretically lead to increased levels of resistance in pregnant people taking INSTIs, no studies have shown altered resistance profiles among pregnant patients [87].

Regarding the teratogenic effects of INSTIs, the most well-documented concern is that of dolutegravir and neural tube defects. In 2018, an observational study in Botswana resulted in a safety signal being released by WHO after investigators found higher rates of neural tube defects among women taking dolutegravir from conception, as compared to women taking non-dolutegravir ARV regimens [80, 91]. However, analysis of final data from this cohort demonstrated a non-significant increased rate of only 0.2%, after which WHO reversed its statement and recommended dolutegravir as a first-line treatment for all individuals, including pregnant people [80, 92••]. Other INSTIs, such as raltegravir and elvitegravir, have not been found to increase rates of congenital anomalies [93].

Overall, INSTIs are considered safe for use in pregnancy. A few studies have found increased rates of hypertensive disease during pregnancy compared to pregnant people on ARV regimens that did not contain INSTIs, but these findings have not been replicated [94, 95].

While INSTIs are a well-tolerated antiretroviral class, there are some common side effects. All INSTIs can cause mild creatinine elevations, which should be considered when used in patients with chronic kidney disease [96]. Another documented side effect of INSTIs is increased weight gain among non-pregnant people [97]; this trend has also been seen among pregnant women, with one study finding 2 kg of excess weight gain comparing people taking dolutegravir versus efavirenz [98]. Notably, several studies have shown increased rates of neuropsychiatric effects, such as depressive symptoms and anxiety in people taking dolutegravir, so this should be considered for patients with a history of neuropsychiatric illness [99].

In summary, dolutegravir, bictegravir, and raltegravir are the only INSTIs recommended for use in pregnant people, with dolutegravir being preferred in light of its once-daily dosing, higher barrier to resistance, and increased volume and duration of pregnancy safety data.

HIV-1 Capsid Inhibitors

HIV-1 capsid inhibitors are a new class of drugs that interfere with HIV capsid, a protein which acts as a shell to protect HIV's genetic material (HIV RNA), proteins (nucleocapsid), and enzymes (reverse transcriptase and integrase) required for replication. This class of drugs can interfere with HIV capsid at multiple points in the viral life cycle including nuclear transport, virus assembly and release, and capsid assembly [100]. Currently, lenacapavir [101] is the only HIV capsid inhibitor approved by the US Food and Drug Administration (FDA). It was approved in December 2022 to be used in combination with other ARV drugs for the treatment of multidrug-resistant HIV-1 infection [102]. Currently, there are no pregnancy-specific data available for lenacapavir. The ongoing Women's HIV Prevention Study is evaluating the use of lenacapavir for pre-exposure prophylaxis in adolescent girls and young women living in sub-Saharan Africa. Participants who become pregnant during the study can remain study participants after a reconsent process.

Results from this study are pending [103]. There are currently insufficient human data to recommend or guide the use of lenacapavir in pregnancy.

Conclusion

Selecting ARV regimens in pregnancy is complex and requires consideration of physiologic changes of pregnancy, pharmacokinetic studies, resistance and efficacy profiles, tolerability and frequency of adverse effects, teratogenicity, and maternal, neonatal, and pregnancy outcomes. Based on these factors, medications are classified for use in pregnancy. *Preferred* and *alternative* ARV regimens for initiation in ARV-naïve pregnant patients are included in Table 1 as an example. A balance must be attempted between choosing the "safest" regimen (with the acknowledgment that research including pregnant people is limited and often delayed compared to the general population) and understanding the risks of changing regimens during an extremely sensitive and high-risk time for perinatal transmission. Regimens with more data may be selected for patients initiating ARV for the first time, but for the vast majority of pregnant people who are on well-tolerated ARV and have achieved viral suppression, medications should be continued. Data is constantly evolving, and providers who manage ARV in pregnancy should liberally utilize national resources like the national guidelines (https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new) and contact the perinatal HIV hotline (888–448–8765, https://nccc.ucsf.edu/clinician-consultation/perinatal-hiv-aids/) to discuss complicated cases.

Data Availability

There is no primary data for this paper.

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• Of importance

•• Of major importance

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Table 1

Recommended antiretroviral regimens for initiation in *antiretroviral-naive* pregnant patients

NRTI*	NNRTI	PI	INSTI
ABC/3TC	*EFV + preferred dual NRTI*	*DRV/r BID + preferred dual NRTI*	**DTG + preferred dual NRTI**
TAF/FTC, TAF/3TC, TDF/FTC, TDF/3TC	*RPV + preferred dual NRTI*	*ATV/r + preferred dual NRTI*	*RAL BID + preferred dual NRTI*
ZDV/3TC BID			*BIC/FTC/TAF*

Bold: preferred regimens, italic: alternative regimens.

Adapted from Table 6 What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naïve. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/perinatal-hiv/tables-perinatal.pdf

BID twice daily dosing in pregnancy, *ABC* abacavir, *ATV/r* atazanavir/ritonavir, *BIC* bictegravir, *DRV/r* darunavir/ritonavir, *DTG* dolutegravir, *EFV* efavirenz, *FTC* emtricitabine, *RAL* raltegravir, *RPV* rilpivirine, *TAF* tenofovir alafenamide, *TDF* tenofovir disoproxil fumarate, *ZDV* zidovudine, *3TC* lamivudine

* Dual NRTI combinations must be combined with a third agent from another category