

Efavirenz (*Sustiva*)

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Drug Summary

Efavirenz, a non-nucleoside reverse transcriptase inhibitor (NNRTI), was an important part of initial combination antiretroviral therapy for many years, especially as a component of the single-tablet regimen efavirenz-tenofovir disoproxil fumarate (DF)-emtricitabine. More recently, efavirenz has largely fallen out of favor and has been replaced by newer agents that have are generally more tolerable. The primary concern regarding efavirenz is the risk of neuropsychiatric adverse effects, including depression, attempted suicide, completed suicide, sleep disturbances, vivid dreams, grogginess, and disorientation. In addition, efavirenz may cause unfavorable changes in lipid parameters. For these reasons, in the United States efavirenz is no longer designated as a recommended option for initial antiretroviral therapy and most clinicians have a low threshold to switch from efavirenz to a newer agent if the patient is experiencing any intolerance to efavirenz. Concerns have been raised regarding potential teratogenicity related to the use of efavirenz in pregnancy, based on early reports of neural tube defects, though that risk has not been confirmed in larger trials and systematic reviews. Efavirenz has a relatively low barrier to resistance, but the mutations that commonly occur carry less cross-resistance with other NNRTI's as compared to the typical rilpivirine mutations.

Key Clinical Trials

Early clinical trials showed efavirenz plus two NRTIs to have superior virologic efficacy as compared to early protease inhibitors (such as indinavir) plus two NRTIs [[006](#)] or as compared to triple-NRTI regimens [[ACTG 5095](#)]. A trial that randomized participants to one of four initial antiretroviral regimens (efavirenz plus either tenofovir DF-emtricitabine or abacavir-lamivudine, or ritonavir-boosted atazanavir plus either tenofovir DF-emtricitabine or abacavir-lamivudine) demonstrated equivalent virologic suppression rates between efavirenz and boosted atazanavir [[ACTG 5202](#)]. For treatment-naïve individuals, the combination of efavirenz plus two NRTIs showed equivalent virologic efficacy to the combination of the NNRTI rilpivirine plus two NRTIs [[ECHO \(C209\)](#)] and [[THRIVE \(C215\)](#)]. Efavirenz plus two NRTIs has been compared to several integrase-inhibitor based initial regimens, including raltegravir plus two NRTI's [[STARTMRK](#)], elvitegravir-cobicistat-tenofovir DF-emtricitabine [[GS-236-0102 \(Study 102\)](#)], and dolutegravir plus two NRTIs [[SINGLE](#)]; the raltegravir and dolutegravir-based regimens demonstrated superior virologic efficacy and the elvitegravir-based

regimen was found to have non-inferior virologic efficacy. Results of these trials also showed that the tolerability of the rilpivirine-based and integrase inhibitor-based regimens was better than that of the efavirenz-based regimen.

Adverse Effects

Efavirenz can cause substantial neuropsychiatric adverse effects. An analysis of four randomized controlled studies of initial antiretroviral therapy regimens found that use of efavirenz-tenofovir DF-emtricitabine was associated with double the rates of suicidality (attempted or completed suicide) compared with use of other regimens. Efavirenz can also cause less serious, but bothersome, neuropsychiatric symptoms, such as insomnia, dizziness, and vivid dreams. It also can cause rash and rarely hepatotoxicity; these both may be severe. The potential for efavirenz to cause neural tube defects in fetuses exposed to efavirenz during the first trimester has been questioned and, despite early reports, has not been confirmed by larger studies and reviews.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), the fixed-dose combination **efavirenz**-tenofovir DF-emtricitabine or **efavirenz** plus a preferred two-NRTI backbone is designated as an Alternative NNRTI Regimen in the category Alternative Initial Regimens in Pregnancy.

- For additional information regarding the safety and toxicity of efavirenz in pregnancy see the HHS Perinatal Guidelines summary on [Efavirenz](#).
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Resistance

For a listing of the most common clinically significant mutations associated with efavirenz (EFV) resistance, see the [NNRTI Resistance Notes on the Stanford University HIV Drug Resistance Database](#).

Key Drug Interactions

For complete information on efavirenz-related drug interactions, see the [Drug Interactions section in the Efavirenz \(Sustiva\) Prescribing Information](#).

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<https://www.hiv.uw.edu/page/treatment/drugs/efavirenz>