Efavirenz-Tenofovir DF-Emtricitabine (*Atripla*)

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Drug Summary

Efavirenz-tenofovir DF-emtricitabine was the first single-tablet regimen approved for treatment of HIV infection. After approval by the FDA in 2006, it was prescribed widely. In recent years, however, it has fallen out of favor and been replaced by newer, more tolerable regimens. The primary concern regarding this combination is that the efavirenz component may cause serious psychiatric adverse effects. In addition, efavirenz can cause other milder central nervous system side effects. For these reasons, in the United States this combination is no longer recommended for initial antiretroviral therapy and most clinicians have a low threshold for switching efavirenz-tenofovir DF-emtricitabine to another regimen, unless the HIV RNA is continuously suppressed and the patient clearly is tolerating it with no side effects. Concerns have been raised about potential teratogenicity related to the use of efavirenz during pregnancy based on early reports of neural tube defects, but that risk has not been confirmed in larger trials and systematic reviews.

Key Clinical Trials

For treatment-naïve individuals, the combination of efavirenz plus tenofovir DF-emtricitabine showed equivalent virologic efficacy to rilpivirine plus tenofovir DF-emtricitabine [ECHO] and [StaR]; in these trials, fewer participants in the efavirenz plus tenofovir DF-emtricitabine arm developed resistance-associated mutations, but more had more adverse effects and discontinued treatment. When compared with doravirine-tenofovir DF-lamivudine in treatment-naïve persons, virologic responses were similar [Drive Ahead]. In other initial therapy trials, efavirenz plus tenofovir DF-emtricitabine has been compared to several integrase inhibitor-based initial regimens, including raltegravir plus tenofovir DF-emtricitabine [StartMrk], dolutegravir plus abacavir-lamivudine [Single], or elvitegravir-cobicistat-tenofovir DF-emtricitabine [Study 102]; 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 demonstrated better tolerability of the integrase inhibitor combinations as compared to the efavirenz combination.
**Adverse Effects**

Efavirenz can cause serious psychiatric side effects. A study that compared the use of efavirenz-tenofovir DF-emtricitabine to other initial regimens documented double the rates of suicidality (suicidal ideation or intent) in those taking efavirenz-based therapy. Efavirenz can also cause other neuropsychiatric symptoms, such as insomnia, dizziness, and vivid dreams, as well as rash or hepatic toxicity, both of which rarely can be severe. Efavirenz typically has unfavorable effects on lipids and can lower vitamin D levels. Tenofovir DF can cause renal proximal tubule wasting and reduced bone mineral density. Emtricitabine is very well tolerated and causes few adverse effects.

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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](https://hivdb.stanford.edu/ resistance_notes.html).

For a listing of the most common clinically significant mutations associated with tenofovir DF (TDF) and/or emtricitabine (FTC) resistance, see the [NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database](https://hivdb.stanford.edu/ resistance_notes.html).

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**Key Drug Interactions**


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