Efavirenz-Tenofovir disoproxil fumarate-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 In recent years, however, it has fallen out of favor and been replaced by newer, more tolerable regimens.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.

Guidelines for use in Antiretroviral-Naïve Patients

In the July 14, 2016 version of the HHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, **efavirenz-tenofovir DF-emtricitabine** is designated as listed below for treatment-naïve patients:

RECOMMENDED Regimen Options

- NOT listed

ALTERNATIVE Regimen Options

- **Efavirenz-tenofovir DF-emtricitabine** (**BI**)

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 (C209)] and [STaR (GS-264-0110)]; 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. 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-emtrictabine [GS-236-0102 (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. Tenofovir DF can cause renal proximal tubule wasting and reduced bone mineral density. Emtricitabine is very well tolerated and causes few adverse effects.

Use In Pregnancy

In the October 26, 2016 version of the HHS Perinatal Treatment Guidelines for Initial Combination Regimens for Antiretroviral-Naïve Pregnant Women, the fixed-dose regimen **efavirenz-tenofovir DF-emtricitabine** is designated as an Alternative Initial Regimen (efavirenz plus two NRTI backbone). The efavirenz-tenofovir DF-emtricitabine package insert includes a warning that pregnancy should be avoided by women who use efavirenz, due to concern regarding potential neural tube defects with efavirenz use in the first trimester. However, the most recent HHS Perinatal Treatment Guidelines have removed this caution because data have not confirmed efavirenz-associated teratogenicity.

- For additional information regarding the safety and toxicity of efavirenz-tenofovir DF-emtricitabine in pregnancy see the HHS Perinatal Guidelines summaries on Efavirenz, Tenofovir DF, and Emtricitabine.

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 .

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.

Key Drug Interactions

For complete information on efavirenz-tenofovir disoproxil fumarate-emtricitabine-related drug interactions, see the Drug Interactions section in the Efavirenz-Tenofovir disoproxil fumarate-Emtricitabine (*Atripla*) Prescribing Information.

No Clinical Trials Available

We do not currently have any clinical trials on file for this drug.

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https://www.hiv.uw.edu/page/treatment/drugs/efavirenz-tenofovir-disoproxil-fumarate-emtricitabine