Rilpivirine-Tenofovir alafenamide-Emtricitabine *(Odefsey)*

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Drug Summary

Rilpivirine-tenofovir alafenamide-emtricitabine is a single-tablet regimen option for certain treatment-naïve individuals. This single-tablet regimen is generally well tolerated, but several important factors limit its use. Rilpivirine-tenofovir alafenamide-emtricitabine should not be offered to individuals with a pretreatment HIV RNA level above 100,000 copies/mL or pretreatment CD4 count less than 200 cells/mm^3 because virologic response rates are lower in these patients. In addition, it is contraindicated for individuals who are taking a proton pump inhibitor and it must be taken with a meal. It is approved for use in the setting of stable mild to moderate renal insufficiency (creatinine clearance as low as 30 mL/min). A similar option with a different tenofovir component (rilpivirine-tenofovir DF-emtricitabine) is also available.

Key Clinical Trials

The FDA approval of rilpivirine-tenofovir alafenamide-emtricitabine was based on extrapolation from prior studies that used rilpivirine-tenofovir DF-emtricitabine or tenofovir alafenamide-based regimens. The rilpivirine-tenofovir DF-emtricitabine studies included (1) pooled data in the ECHO and THRIVE studies involving 550 treatment-naïve patients and (2) data from 317 carefully selected patients with virologic control who switched from a virologically suppressive PI-based regimen to rilpivirine-tenofovir DF-emtricitabine [SPIRIT]. The tenofovir alafenamide-related studies showed excellent virologic and safety data from (1) treatment-naïve patients who received elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine [Study 104/111], (2) participants who had virologic suppression on a tenofovir-DF-based regimen with no significant antiretroviral resistance mutations and who switched to elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine [Study 109], and (3) participants with virologic suppression and a creatinine clearance of 30 to 69 mL/min who switched to elvitegravir-tenofovir alafenamide-emtricitabine [Study 112]. Following the FDA approval of rilpivirine-tenofovir alafenamide-emtricitabine, several clinical trials have evaluated a switch to the fixed-dose combination rilpivirine-tenofovir alafenamide-emtricitabine from either fixed-dose combination efavirenz-tenofovir DF-emtricitabine [GS-366-1160] or fixed-dose rilpivirine-tenofovir DF-emtricitabine [GS-366-1216]. These studies have demonstrated that patients who are suppressed on these specific pre-switch antiretroviral therapy regimens can safely switch to rilpivirine-tenofovir alafenamide-emtricitabine and

this switch leads to improvement in markers of renal proximal tubulopathy and bone turnover.

Adverse Effects

Rilpivirine-tenofovir alafenamide-emtricitabine is generally well tolerated. Side effects can include headache, insomnia, depression, rash, or elevation of hepatic transaminases. Supratherapeutic doses of rilpivirine can cause QT prolongation; therefore, caution should be used when prescribing rilpivirine with other QT prolonging agents or other medications that may significantly increase levels of rilpivirine; if rilpivirine must be used in either of these situations, QT should be monitored.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **rilpivirine-tenofovir alafenamide-emtricitabine** is designated in the category of Insufficient Data in Pregnancy to Recommend Routine Use in Initial Regimens for Antiretroviral-Naïve Women.

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

Resistance

For a listing of the most common clinically significant mutations associated with rilpivirine (RPV) 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 alafenamide (TAF) and/or emtricitabine (FTC) resistance, see the NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database. Note that both tenofovir alafenamide and tenofovir disoproxil fumarate are converted to tenofovir disphophate, the active form of the drug. Thus, resistance mutations for tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are the same.

Key Drug Interactions

For complete information on rilpivirine-tenofovir alafenamide-emtricitabine-related drug interactions, see the Drug Interactions section in the Rilpivirine-Tenofovir alafenamide-Emtricitabine (*Odefsey*) Prescribing

Information.