Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine (Genvoya)

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Drug Summary

Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine is an effective and well-tolerated single-tablet once daily combination regimen. Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine has been studied as first-line therapy, as part of a simplification option for carefully selected heavily treatment-experienced individuals, and as therapy for individuals with HIV-hepatitis B coinfection. Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine differs from the fixed-dose combination elvitegravir-cobicistat-tenofovir disoproxil fumarate (DF)-emtricitabine only by the tenofovir components of the two regimens. Tenofovir alafenamide, when compared with tenofovir DF, has lower risk of causing nephroxicity and loss of bone mineral density. Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine is approved for use in patients with stable mild to moderate renal insufficiency (creatinine clearance as low as 30 mL/min), thereby providing another advantage over regimens that include tenofovir DF (which requires dose reduction in the setting of renal impairment). The main disadvantage and clinical limitation of elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine is related to gastrointestinal side effects and drug interactions, which are primarily due to the cobicistat component.

Key Clinical Trials

Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine demonstrated non-inferior virologic efficacy when compared with elvitegravir-cobicistat-tenofovir DF-emtricitabine [Study 104/111]. A switch to elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine in patients with HIV suppression on a stable antiretroviral regimen (either elvitegravir-cobicistat-tenofovir DF-emtricitabine, tenofovir DF-emtricitabine plus atazanavir plus ritonavir, or tenofovir DF-emtricitabine plus efavirenz) found the elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine regimen to be as effective as elvitegravir-cobicistat-tenofovir DF-emtricitabine and superior in terms of proportion of patients with virologic suppression when compared with the other regimens [Study 109]. In addition, patients taking the elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine regimen had relatively favorable markers of renal proximal tubule wasting and bone density loss. In a separate study, a switch from a variety of first-line regimens to elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine in the setting of mild-moderate renal insufficiency (creatinine clearance 30 to 69 mL/min) was
also effective in maintaining HIV suppression and led to improvements in markers of renal proximal tubule wasting and bone mineral density [Study 112]. In a study of heavily treatment-experienced individuals with virologic suppression on complex salvage regimens that included boosted darunavir (and who had multiclass drug resistance that met certain pre-specified parameters), simplification to a two-pill daily combination of elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine plus darunavir was superior to continuing current therapy [Study 119]. In an open-label, non-randomized study that enrolled patients with well controlled HIV and hepatitis B coinfection, all participants switched antiretroviral therapy to elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine and HIV and hepatitis B virologic control was maintained [Study 1249].

**Resistance**

For a listing of the most common clinically significant mutations associated with elvitegravir (EVG) resistance, see the [INSTI Resistance Notes on the Stanford University HIV Drug Resistance Database](https://www.hiv.uw.edu/page/treatment/drugs/elvitegravir-cobicistat-tenofovir-alafenamide-emtricitabine).

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](https://www.hiv.uw.edu/page/treatment/drugs/elvitegravir-cobicistat-tenofovir-alafenamide-emtricitabine). Note that both tenofovir alafenamide and tenofovir disoproxil fumarate are converted to tenofovir disphosphate, 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 elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine-related drug interactions, see the [Drug Interactions section in the Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine (Genvoya) Prescribing Information](https://www.hiv.uw.edu/page/treatment/drugs/elvitegravir-cobicistat-tenofovir-alafenamide-emtricitabine).