

# 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 older fixed-dose combination elvitegravir-cobicistat-tenofovir disoproxil fumarate (DF)-emtricitabine only by the tenofovir components of the two regimens. Tenofovir alafenamide, when compared to tenofovir DF, improves markers of renal proximal tubule wasting and causes less 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 primary potential disadvantages and clinical limitations of elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine are gastrointestinal side effects and drug interactions, which are primarily due to the cobicistat component.

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## Key Clinical Trials

Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine demonstrated non-inferior virologic efficacy when compared with elvitegravir-cobicistat-tenofovir DF-emtricitabine [[GS-292-0104/GS-292-0111 \(Study 104/111\)](#)]. 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 equally effective as elvitegravir-cobicistat-tenofovir DF-emtricitabine and superior in terms of proportion of patients with virologic suppression when compared with the other regimens [[GS-292-0109 \(Study 109\)](#)]. In addition, patients on 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 also led to improvements in markers of renal proximal tubule wasting and bone mineral density [[GS-292-0112 \(Study 112\)](#)]. 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 [[GS-292-0119 \(Study 119\)](#)]. 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 [[GS-292-1249 \(Study 1249\)](#)].

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## Adverse Effects

Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine can cause nonspecific symptoms such as fatigue, headache, malaise, nausea, and diarrhea. The emtricitabine and elvitegravir components of the regimen generally cause very few side effects. Gastrointestinal side effects are one of the most common adverse events and are likely caused by the cobicistat component. Available data on the tenofovir alafenamide component, as compared with tenofovir DF, show lower markers of renal proximal tubule wasting, favorable effects on bone mineral density (less loss of bone mineral density when started as initial therapy and improvements in bone mineral density after a change from tenofovir DF-emtricitabine to tenofovir alafenamide-emtricitabine), but unfavorable effects on serum lipid parameters. Long-term follow-up to assess rates of clinical events (such as osteoporotic fractures or cardiovascular events) with tenofovir alafenamide as compared to tenofovir DF or other regimens is lacking. Because elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine contains two medications (tenofovir alafenamide and emtricitabine) that have activity against hepatitis B virus, discontinuation of cobicistat-tenofovir alafenamide-emtricitabine in patients with chronic hepatitis B infection can potentially cause a severe acute exacerbation of hepatitis B, including an abrupt rise in hepatic aminotransferase levels.

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## Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine** is listed in the category of Not Recommended for Initial ART in Pregnancy, because of concerns of virologic breakthrough due to lowered levels of elvitegravir and cobicistat in the second and third trimesters of pregnancy.

- For additional information regarding the safety and toxicity of elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine in pregnancy see the HHS Perinatal Guidelines summaries on [Elvitegravir](#), [Cobicistat](#), [Tenofovir alafenamide](#), and [Emtricitabine](#).
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## 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](#).

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 disphosphate, the active form of the drug. Thus, resistance mutations for tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are the same.

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## 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](#).