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 [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 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 [GS-292-0109 (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 [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 and less loss of bone mineral density. Tenofovir alafenamide causes
increases in LDL and HLD compared with tenofovir DF, but the clinical significance of these
differences in lipid parameters remains unclear. Long-term follow-up to assess rates of clinical
adverse events (such as osteoporotic fractures or cardiovascular events) with tenofovir alafenamide
does not suggest that it is different 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 elvitegravir-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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**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.