

Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine (*Symtuza*)

Table of Contents

- [Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine *Symtuza* Editor's Summary](#)
- [Drug Summary](#)
- [Key Clinical Trials](#)
- [Adverse Effects](#)
- [Use In Pregnancy](#)
- [Key Drug Interactions](#)

Drug Summary

The fixed-dose combination tablet darunavir-cobicistat-tenofovir alafenamide-emtricitabine is a single-tablet regimen that can be considered for treatment-naïve or certain treatment-experienced adults living with HIV. This single-tablet regimen offers a one pill daily regimen with high barrier to resistance (due to the darunavir-cobicistat), with potentially less renal and bone toxicity as compared to regimens that include tenofovir DF; however, it has potential gastrointestinal adverse effects and drug-drug interactions, primarily due to the cobicistat component. In clinical trials, darunavir-cobicistat-tenofovir alafenamide-emtricitabine was compared to darunavir-cobicistat plus tenofovir DF-emtricitabine as initial therapy for treatment-naïve individuals and found to be equally effective in terms of viral suppression. A switch to the fixed-dose combination tablet was also compared to continuing a boosted protease inhibitor plus tenofovir DF-emtricitabine and again determined to have equivalent efficacy. The FDA has approved darunavir-cobicistat-tenofovir alafenamide-emtricitabine as a complete regimen for treatment-naïve individuals or treatment-experienced individuals who have a suppressed HIV RNA level on a stable regimen for at least 6 months and no resistance to darunavir or tenofovir.

Key Clinical Trials

A phase 3 trial in treatment-naïve individuals compared the fixed-dose single-tablet regimen darunavir-cobicistat-tenofovir alafenamide-emtricitabine with the regimen darunavir-cobicistat plus tenofovir DF-emtricitabine emtricitabine [[AMBER](#)]. In this trial, 725 treatment-naïve adults were randomized in 1:1 fashion to the two arms. At week 48, the proportion with HIV RNA level below 50 copies/mL was not statistically different (91.4% in the darunavir-cobicistat-tenofovir alafenamide-emtricitabine arm and 88.4% in the darunavir-cobicistat plus tenofovir DF-emtricitabine arm). Markers of bone mineral density and renal tubule wasting were better in the group who took the single-tablet, tenofovir alafenamide-containing regimen.

A phase 3 switch study enrolled individuals taking a boosted protease inhibitor plus tenofovir DF-

emtricitabine and randomized participants to continue the regimen or switch to darunavir-cobicistat-tenofovir alafenamide-emtricitabine [EMERALD]. Overall, 1,141 enrollees were randomized in 2:1 fashion to the switch arm versus continue baseline therapy. All participants had a suppressed HIV RNA level and individuals were excluded if they had resistance mutations known to affect the activity of darunavir or tenofovir (past virologic failure on a non-darunavir-containing regimen was allowed). At 48 weeks, rates of virologic rebound failure were low and statistically different between the two arms. Overall tolerability was similar between the two groups, though markers of bone mineral density loss and renal tubulopathy favored the tenofovir alafenamide-containing single tablet regimen.

Adverse Effects

Common adverse effects with tenofovir alafenamide-emtricitabine-darunavir-cobicistat include nausea, diarrhea, and other gastrointestinal symptoms, which commonly occur secondary to darunavir or cobicistat. Darunavir may also cause headache, rash, elevation of hepatic aminotransferase levels, and worsening of serum lipid levels. Darunavir contains a sulfonamide moiety and thus should be used cautiously in individuals with a history of sulfonamide allergy. Cobicistat blocks tubular secretion of creatinine and thereby causes a mild benign elevation of serum creatinine and reduction of estimated GFR (with no effect on true or measured GFR). Emtricitabine infrequently causes adverse effects. The primary advantage of tenofovir alafenamide over tenofovir DF is reduced adverse effects related to proximal tubule toxicity and bone mineral density loss; the long-term clinical significance of these differences is not yet known. For more on potential adverse effects, see the summary for each individual component.

Use In Pregnancy

Darunavir-cobicistat-tenofovir alafenamide-emtricitabine is not recommended for use in pregnancy.

Key Drug Interactions

For complete information on darunavir-cobicistat-tenofovir alafenamide-emtricitabine-related drug interactions, see the [Drug Interactions section in the Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine \(Symtuza\) Prescribing Information](#).

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PDF created November 18, 2018, 11:19 am

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