

Atazanavir-Cobicistat (*Evotaz*)

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Drug Summary

Atazanavir-cobicistat is a fixed-dose combination pill consisting of a protease inhibitor (atazanavir) and a pharmacologic booster (cobicistat). Until recently, atazanavir boosted with ritonavir (another pharmacologic booster) was often used with two nucleoside reverse transcriptase inhibitors (NRTIs) for initial antiretroviral therapy, but in recent years atazanavir has largely been replaced by more tolerable anchor agents. The fixed-dose combination atazanavir-cobicistat offers a one-pill alternative to the two pills of atazanavir plus ritonavir. The atazanavir component of this fixed-dose combination can cause several significant adverse effects, including indirect hyperbilirubinemia, kidney stones, and gallstones. Cobicistat typically causes a benign small increase in serum creatinine. In addition, cobicistat can cause significant drug interactions. Atazanavir levels can be significantly reduced with acid-suppressing agents.

Key Clinical Trials

A randomized, double-blind, controlled trial compared atazanavir-cobicistat plus two NRTIs to atazanavir plus ritonavir plus two NRTIs and found it to be noninferior in terms of virologic suppression rates as well as safety and tolerability [[Study 114](#)]. Another trial enrolled individuals with suppressed HIV RNA levels and creatinine clearance 50 to 89 mL/min while taking a regimen that included ritonavir-boosted atazanavir or ritonavir-boosted darunavir, each with 2 NRTIs; in this open-label, noncomparative trial, all participants were switched from ritonavir to cobicistat and 89% maintained suppressed HIV RNA levels virologically at 96 weeks [[Study 118](#)]. Mild, nonprogressive increases in serum creatinine were noted early after the switch (as expected with cobicistat), but no cases of renal proximal tubulopathy developed.

Adverse Effects

Atazanavir blocks the enzyme that conjugates bilirubin and therefore causes a mild, usually asymptomatic indirect hyperbilirubinemia; occasionally, this leads to jaundice, which is not dangerous and resolves after discontinuation of atazanavir. Atazanavir can also cause an increase in the PR interval of the electrocardiogram, gastrointestinal symptoms such as nausea and diarrhea, and, less commonly, nephrolithiasis, cholelithiasis, rash, and elevation of hepatic transaminases. Boosted atazanavir can worsen serum lipid parameters, though is better in this regard than earlier generation protease inhibitors. 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).

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **atazanavir-cobicistat** is designated in the category of Not Recommended for Initial ART in Pregnancy. This recommendation is based on the limited data on atazanavir-cobicistat in pregnancy.

- For additional information regarding the safety and toxicity of atazanavir-cobicistat in pregnancy see the HHS Perinatal Guidelines summaries on [Atazanavir](#) and [Cobicistat](#).
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Resistance

For a listing of the most common clinically significant mutations associated with atazanavir-cobicistat (ATV-COBI) resistance, see the [PI Resistance Notes on the Stanford University HIV Drug Resistance Database](#).

Key Drug Interactions

For complete information on atazanavir-cobicistat-related drug interactions, see the [Drug Interactions section in the Atazanavir-Cobicistat \(Evotaz\) Prescribing Information](#).

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<https://www.hiv.uw.edu/page/treatment/drugs/atazanavir-cobicistat>