

Atazanavir (*Reyataz*)

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Drug Summary

Atazanavir is a protease inhibitor that, when given with a pharmacokinetic enhancer (ritonavir or cobicistat), is a potent, once-daily anchor agent for antiretroviral therapy. In the past, it was prescribed frequently for initial treatment, but in recent years several newer and better-tolerated anchor drugs have largely replaced atazanavir in clinical practice. Atazanavir causes indirect hyperbilirubinemia that can lead to jaundice, which is benign but can be cosmetically bothersome, especially with icterus; it can also cause nephrolithiasis and gallstones. In addition, concomitant use of certain acid-suppressive agents can significantly decrease absorption of atazanavir. If a patient is taking atazanavir as part of combination antiretroviral therapy and is tolerating it well with consistently suppressed HIV RNA levels, it is not necessary to change atazanavir to another agent, though most clinicians have a low threshold to switch the regimen if the patient has troublesome side effects. Atazanavir can be given either with or without a pharmacokinetic booster, though current guidelines recommend that it be combined with a pharmacokinetic enhancer and advise against use of unboosted atazanavir.

Key Clinical Trials

Atazanavir has primarily been studied in treatment-naïve individuals. A randomized clinical trial of initial antiretroviral therapy compared once-daily ritonavir-boosted atazanavir to twice-daily lopinavir-ritonavir, each with tenofovir DF-emtricitabine, and found equivalent virologic efficacy [[CASTLE](#)]. Another randomized trial of treatment-naïve adults compared ritonavir-boosted atazanavir, ritonavir-boosted darunavir, and raltegravir, each with tenofovir DF-emtricitabine; in this trial, the atazanavir regimen was inferior to both ritonavir-boosted darunavir and raltegravir; inferiority was primarily caused by a higher rate of adverse effects and treatment discontinuations in the atazanavir arm [[ARDENT](#)]. Investigators also compared initial therapy with ritonavir-boosted atazanavir plus tenofovir DF-emtricitabine to elvitegravir-cobicistat-tenofovir DF-emtricitabine and the two arms demonstrated equivalent virologic suppression rates [[Study 103](#)]. A study of initial therapy in adult women with HIV reported statistically inferior virologic responses with ritonavir-boosted

atazanavir plus two nucleoside reverse transcriptase inhibitors (NRTIs) compared with dolutegravir-abacavir-lamivudine, primarily due to differences in tolerability and discontinuations [[Study 128 \(WAVES\)](#)]. As part of initial therapy, cobicistat-boosted atazanavir was compared to ritonavir-boosted atazanavir and found to be equivalent [[Study 114](#)].

In treatment-experienced adults with prior treatment failure on protease-inhibitor based therapy, unboosted atazanavir plus two NRTIs demonstrated statistically lower rates of virologic suppression compared with lopinavir-ritonavir plus two nucleoside reverse transcriptase inhibitors (NRTIs) [[Study 043](#)], but ritonavir-boosted atazanavir had equivalent efficacy as lopinavir-ritonavir when each were combined with tenofovir DF and one additional NRTI [[Study 045](#)].

Adverse Effects

Atazanavir competitively inhibits an enzyme responsible for the glucuronidation of bilirubin, which frequently causes a mild, asymptomatic indirect hyperbilirubinemia; occasionally this leads to overt icterus, which is not dangerous, but may be disturbing to patients. Jaundice, when it occurs, will resolve after discontinuation of atazanavir. Atazanavir can crystallize in the urinary or biliary tract and cause nephrolithiasis or cholelithiasis. It can also cause an increase in the PR interval of the electrocardiogram, mild-moderate gastrointestinal symptoms such as nausea and diarrhea. Rarely, patients taking atazanavir will develop rash or elevation of hepatic aminotransferase levels. Ritonavir-boosted atazanavir can worsen serum lipid parameters, though is better in this regard than earlier-generation protease inhibitors.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), ritonavir-boosted **atazanavir** plus a preferred two-NRTI backbone is designated as one of the Preferred Protease Inhibitor Regimens in the category Preferred Initial Regimens in Pregnancy. In pregnancy, atazanavir cannot be administered with proton pump inhibitors.

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

Resistance

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

Key Drug Interactions

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