

Darunavir (*Prezista*)

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Drug Summary

Darunavir is a potent, later-generation protease inhibitor that must be combined with a pharmacokinetic booster, either cobicistat or ritonavir. Boosted darunavir is an option for initial antiretroviral therapy and it is also a common component of salvage regimens for treatment-experienced individuals. Darunavir has a unique resistance pathway and retains activity following the development of drug resistance with most other protease inhibitors, with a notable exception that virologic failure on fosamprenavir can result in cross resistance with darunavir. In addition, darunavir has a high barrier to drug resistance, and when patients taking darunavir develop virologic failure, darunavir-associated resistance mutations usually are not present. For treatment-naïve patients, ritonavir-boosted darunavir is dosed once daily; for treatment-experienced patients, the dosing of darunavir is determined by whether or not darunavir-associated mutations are present. If they are absent, ritonavir-boosted darunavir can be dosed once daily, but if darunavir-associated mutations are present, the dosing should be twice daily. The fixed-dose combination of darunavir-cobicistat should only be used when once daily darunavir dosing is appropriate. The primary disadvantages of darunavir include moderate gastrointestinal side effects, potential for drug interactions, and possible adverse reactions in individuals with history of severe sulfa allergy (darunavir contains a sulfonamide moiety).

Guidelines for use in Antiretroviral-Naïve Patients

In the July 14, 2016 version of the HHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, **darunavir** is designated as listed below for treatment-naïve patients:

RECOMMENDED Regimen Options

- **Darunavir** plus ritonavir plus tenofovir DF-emtricitabine (**AI**)
- **Darunavir** plus ritonavir plus tenofovir alafenamide-emtricitabine (**AII**)

ALTERNATIVE Regimen Options

- **Darunavir**-cobicistat plus abacavir-lamivudine—only if HLA-B*5701 negative (**BIII**)
 - **Darunavir** plus ritonavir plus abacavir-lamivudine- only if HLA-B*5701 negative (**BII**)
 - **Darunavir**-cobicistat plus tenofovir DF-emtricitabine (**BII**)
 - **Darunavir**-cobicistat plus tenofovir alafenamide-emtricitabine (**BII**)
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Key Clinical Trials

Darunavir has been extensively studied in treatment-naïve and treatment-experienced individuals. In antiretroviral-naïve adults, a comparison of once-daily ritonavir-boosted darunavir with lopinavir-ritonavir (given once or twice-daily), each with tenofovir DF-emtricitabine, showed similar virologic efficacy between the two arms, except for the subset of participants with pre-treatment HIV RNA levels above 100,000 copies/mL, who achieved higher rates of virologic suppression with ritonavir-boosted darunavir [[ARTEMIS](#)]. In treatment-naïve individuals, a randomized comparison of once-daily ritonavir-boosted darunavir and once-daily dolutegravir, each with two NRTIs, showed that the darunavir arm was inferior, largely due to more side effects and treatment discontinuations [[FLAMINGO](#)]. In a trial of treatment-naïve individuals randomized to ritonavir-boosted darunavir, ritonavir-boosted atazanavir, or raltegravir, each with tenofovir DF-emtricitabine, raltegravir achieved the best virologic outcomes, followed by boosted darunavir, and then boosted atazanavir [[ARDENT \(ACTG 5257\)](#)]. Outcome differences in that trial were largely driven by tolerability. In treatment-experienced individuals with multiclass drug resistance, twice-daily ritonavir-boosted darunavir was compared to other boosted protease inhibitors (each given with an optimized background regimen of NRTIs with or without enfuvirtide); boosted darunavir achieved statistically higher rates of virologic response [[POWER 1 and 2](#)]. A noncomparative trial that included individuals with virologic failure and multiclass drug resistance found high rates of virologic success with a salvage regimen that included ritonavir-boosted darunavir (given twice daily) plus raltegravir plus etravirine [[TRIO](#)]. In treatment-experienced patients with no darunavir-associated mutations but detectable HIV RNA while taking stable antiretroviral therapy, a randomized switch to either once-daily or twice-daily ritonavir-boosted darunavir plus NRTIs resulted in no statistically significant difference in rates of HIV RNA suppression at week 48 [[ODIN](#)]. Several studies demonstrated the efficacy of monotherapy with ritonavir-boosted darunavir as a simplification strategy in patients with previously suppressed HIV RNA levels on a standard three-drug regimen [[MONOI](#)] and [[MONET](#)].

Adverse Effects

Common adverse effects with darunavir (given in conjunction with one of the pharmacologic boosters, ritonavir or cobicistat) include nausea, diarrhea, and other gastrointestinal upset. Darunavir may also cause headache, rash, elevation of hepatic transaminases, or increases in serum lipid parameters. Darunavir contains a sulfonamide moiety and thus should be used cautiously in individuals with a known sulfonamide allergy. Although the rates of allergic reaction with darunavir are higher in individuals with a history of sulfonamide allergy when compared with individuals with no history of sulfonamide allergy, clinically significant reactions occur infrequently. Nonetheless, most experts would avoid use of darunavir in patients with a history of severe sulfonamide allergy, such as a prior incidence of Stevens-Johnson syndrome.

Use In Pregnancy

In the October 26, 2016 version of the HHS Perinatal Treatment Guidelines for Initial Combination Regimens for Antiretroviral-Naïve Pregnant Women, **darunavir** plus ritonavir is designated as one of the Preferred Protease Inhibitor Regimen in the category Preferred Initial Regimens in Pregnancy. The guidelines recommend that boosted darunavir should be dosed twice daily during pregnancy.

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

Resistance

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

Key Drug Interactions

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

No Clinical Trials Available

We do not currently have any clinical trials on file for this drug.

Figures

Figure 1 darunavir-prezista_800mg-tablet



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The most up to date version of this content may be obtained from:

<https://www.hiv.uw.edu/page/treatment/drugs/darunavir>