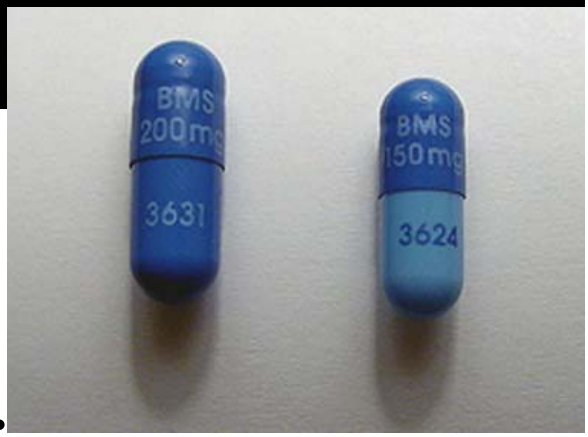
Reyataz (atazanavir)



Reyataz capsules are dark blue (200 mg) or half dark blue and half light blue (150 mg). The capsules are labeled with "BMS," the dose, and a 4-digit number ("3631" for the 200 mg or "3624" for the 150 mg). Dosing may vary. [Not shown: 100-mg capsule, half blue/half white, "3623"].

Also known as: atazanavir sulfate

Background and description. Reyataz is an anti-HIV drug manufactured by Bristol-Myers Squibb Company. The drug is a protease inhibitor (PI). In June 2003, The FDA approved Reyataz for use, in combination with other antiretroviral drugs, in treating HIV.

Dose. Reyataz is supplied in capsules of 100 mg, 150 mg, and 200 mg. Reyataz should be taken once a day at the same time each day. Reyataz should be taken in combination with other HIV drugs. The typical dose of Reyataz is 400 mg once daily. However, data show that 100 mg of Norvir taken with 300 mg of Reyataz achieves higher and more stable levels of Reyataz in the body. This is especially important in PI-experienced patients and *the FDA-approved dose for these patients is 300 mg of Reyataz with 100 mg of Norvir with food once daily*.

The exact dose of Reyataz depends on many factors, including liver function and other HIV drugs taken. If taking Reyataz with either Viread or Sustiva, Norvir must also be taken to help boost Reyataz levels in the body. If taking Reyataz with the buffered (older) formulation of Videx or any antacids, Reyataz should be taken 2 hours before or 1 hour after the Videx or antacids.

Food restrictions. Reyataz should be taken with a meal or snack.

Storage. Reyataz should be stored at room temperature (77ºF). Do not store Reyataz in a damp place such as a bathroom medicine cabinet or near the kitchen sink.

Patient assistance. Bristol-Myers Squibb provides a patient assistance program for those who qualify. For more information, call 800.272.4878.

Side effects. The most common side effects of Reyataz are yellowing of the skin or eyes (increased bilirubin levels), heart rhythm changes (PR interval prolongation/AV block), and diabetes and high blood sugar (hyperglycemia). Patients with a heart condition known as "atrioventricular block" should use caution when using Reyataz and may want to consider an alternative to Reyataz. As a class, PIs are associated with metabolic (mainly sugar and lipid) and morphologic (body shape) changes. However, lipid elevations are not seen as often in patients taking Reyataz (and when present, not at the levels seen with other PIs). Other common side effects of Reyataz taken with other HIV drugs include nausea; headache; rash (can be severe in rare cases); stomach pain; vomiting; diarrhea; depression; fever; increased cough; dizziness; trouble sleeping; pain; tiredness; back pain; numbness, tingling, or burning of the hands or feet; and joint pain. Pregnant women should not take Reyataz.

Drug interactions. Reyataz should not be taken with the following: ergot derivatives such as Cafergot, Migranal, and DHE 45; Halcion (triazolam); Versed (midazolam); Orap (pimozide); Propulsid (cisapride); Camptosar (irinotecan); Vascor (bepridil); and cholesterol-lowering drugs such as Mevacor (lovastatin) or Zocor (simvastatin). In addition, the PI Crixivan should not be taken with Reyataz.

Caution should be used when combining Reyataz with: Rifadin and Rimactane (rifampin), St. John's wort (*Hypericum perforatum*), Viagra (sildenafil), Cialis (tadalafil), Levitra (vardenafil), Lipitor (atorvastatin), medicines for abnormal heart rhythm such as Cordarone (amiodarone), lidocaine, quinidine (also known as Cardioquin, Quinidex, and others), Coumadin (warfarin), tricyclic antidepressants, and medicines to prevent organ transplant rejection. Reyataz should **not** be used with proton-pump inhibitors (which help suppress acid in the stomach) such as Nexium (esomeprazole), Prevacid (lansoprazole), or Prilosec (omeprazole).

Viread lowers the levels of Reyataz in the body. Therefore, boosting once-daily Reyataz (300 mg) with 100 mg of Norvir is recommended when taken with Viread (all as a single daily dose with food). In addition, the following medicines may require a dosing change of either Reyataz or the other medicine: Sustiva, Fortovase or Invirase, Norvir, Mycobutin (rifabutin), Biaxin (clarithromycin), oral contraceptives, antacids, medicines for indigestion, heartburn, or ulcers such as Axid, Pepcid AC, Tagamet, or Zantac, and buffered Videx. Videx EC can be used, but should be taken at a different time than Reyataz.

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Additional info:

Resistance and cross-resistance. Reyataz-resistant samples have been obtained from patients experiencing virologic failure on Reyataz. There were 14 Reyataz-resistant isolates from studies of treatment-naive patients (n=96 evaluable isolates) that showed decreases in susceptibility levels from baseline, and all had an I50L substitution after an average of 50 weeks of therapy (often in combination with an A71V mutation). Phenotypic analysis of the isolates containing the signature mutation I50L showed Reyataz-specific resistance, which coincided with increased susceptibility to other protease inhibitors. In contrast, 89% (32 of 36) of Reyataz-resistant isolates from studies of treatment-experienced patients (n=67 evaluable isolates) showed no evidence of the emergence of the I50L substitution. Instead, these isolates displayed decreased susceptibility to multiple protease inhibitors and contained mutations associated with resistance to multiple protease inhibitors. These mutations occurred at known sites for PI cross-resistance: 84, 90, 71, 88, and 46. The mutations conferred Reyataz resistance and reduced the clinical response to Reyataz. Generally, if PI mutations were present in the patient at baseline, Reyataz resistance developed through mutations associated with resistance to other PIs instead of the I50L mutation. As is generally the case, the more PI mutations present when starting Reyataz, the less likely an effective antiretroviral response was achieved.

Clinical data. Approval for Reyataz was based primarily on 3 efficacy studies. Study AI424-034 was a randomized, double-blind, multicenter trial comparing Reyataz (once daily) to Sustiva (once daily), each in combination with a fixed-dose combination of Epivir (lamivudine) and Retrovir (zidovudine) given twice daily, in 810 antiretroviral treatment-naive patients. The mean baseline CD4 cell count was 321 cells/mm^3 (range: 64 – 1424 cells/mm^3) and the mean baseline plasma HIV-1 RNA level was 4.8 $\log_{10}$ copies/mL (range: 2.2 – 5.9 $\log_{10}$ copies/mL). At baseline, 405 patients were randomized to each arm. Through 48 weeks of therapy, the proportion of responders among patients with high viral loads (ie, baseline HIV RNA $\geq$100,000 copies/mL) was comparable for the Reyataz and efavirenz arms. The mean increase from baseline in CD4 cell count was 176 cells/mm^3 for the Reyataz arm and 160 cells/mm^3 for the Sustiva arm.

Study AI424-008 was a 48-week, randomized, multicenter trial, blinded to dose of Reyataz. The study compared Reyataz at two dose levels (400 mg or 600 mg) once daily to Viracept (nelfinavir) twice daily, each in combination with Zerit (stavudine) and Epivir given twice daily, in 467 antiretroviral treatment-naive patients. The mean baseline CD4 cell count was 295 cells/mm^3 (range: 4 – 1003 cells/mm^3) and the mean baseline plasma HIV-1 RNA level was 4.7 $\log_{10}$ copies/mL (range: 1.8 – 5.9 $\log_{10}$ copies/mL). Through 48 weeks of therapy, the mean increase from baseline in CD4 cell count was 234 cells/mm^3 for the Reyataz 400-mg arm and 211 cells/mm^3 for the Viracept arm. The proportion of responders was 67% in the Reyataz 400-mg arm and 59% in the Viracept arm.

Study AI424-043 is an ongoing, randomized, open-label, multicenter trial comparing Reyataz once daily to Kaletra (lopinavir/ritonavir) twice daily, each in combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs), in 300 patients who experienced virologic failure to only one prior PI-containing regimen. For the 229 patients who have been assessed for efficacy, the mean time of prior exposure to antiretrovirals was 140 weeks for PIs, 180 weeks for NRTIs, and 85 weeks for non-nucleoside reverse transcriptase inhibitors (NNRTIs). The mean baseline CD4 cell count was 318 cells/mm^3 (range: 18 – 1118 cells/mm^3) and the mean baseline plasma HIV-1 RNA level was 4.17 $\log_{10}$ copies/mL (range: 2.60 – 5.87 $\log_{10}$ copies/mL). Through week 24, the proportion of responders (HIV RNA < 400 copies/mL) was 54% in the Reyataz arm and 75% in the Kaletra arm. Thirty-four percent of patients in the Reyataz arm experienced HIV RNA levels <50 copies/mL, while 50% of patients in the Kaletra arm experienced these levels. The time-weighted average change from baseline HIV RNA in the Reyataz arm was -1.73 log versus -2.16 log in the Kaletra arm.

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