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- **Immune reconstitution syndrome** has been reported in patients treated with combination antiretroviral therapy, including REYATAZ. **Increased bleeding** has been reported **in hemophiliacs** treated with protease inhibitor therapy. Various degrees of **cross-resistance** among protease inhibitors have been observed.
- REYATAZ should be used with caution in patients with mild to moderate hepatic impairment. REYATAZ should not be used in patients with **severe hepatic impairment** (Child-Pugh Class C) or in treatment-experienced patients with **end-stage renal disease managed with hemodialysis**. REYATAZ/ritonavir has not been studied in patients with hepatic impairment and is not recommended.

The **most common moderate or severe adverse reactions** were as follows, regardless of causality:

- ***In treatment-naive adult patients*** (≥2%): nausea (4-14%), jaundice/scleral icterus (5-7%), rash (3-7%), headache (1-6%), abdominal pain (4%), vomiting (3-4%), peripheral neurologic symptoms (<1-4%), diarrhea (1-3%), insomnia (<1-3%), and dizziness (<1-2%).
- ***In treatment-experienced adult patients*** (≥2%): jaundice/scleral icterus (9%), myalgia (4%), diarrhea (3%), nausea (3%), depression (2%), and fever (2%).
- ***In pediatric patients*** (≥5%): cough (21%), fever (18%), jaundice/scleral icterus (15%), rash (14%), vomiting (12%), diarrhea (9%), headache (8%), peripheral edema (7%), extremity pain (6%), nasal congestion (6%), oropharyngeal pain (6%), wheezing (6%), and rhinorrhea (6%).

References: 1. Molina JM, Andrade-Villanueva J, Echevarria J, et al. Once-daily atazanavir/ritonavir versus twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1-infected patients: 48 week efficacy and safety results of the CASTLE study. *Lancet.* 2008;372:646-655. **2.** Molina JM, Villanueva JA, Echevarria J, et al. Once-daily atazanavir/ritonavir compared with twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1-infected patients: 96-week efficacy and safety results of the CASTLE study. *J Acquir Immune Defic Syndr.* 2010;53:323-332. **3.** Squires K, Lazzarin A, Gatell JM, et al. Comparison of once-daily atazanavir with efavirenz, each in combination with fixed-dose zidovudine and lamivudine, as initial therapy for patients infected with HIV. *J Acquir Immune Defic Syndr.* 2004;36:1011-1019. **4.** Johnson M, Grinsztejn B, Rodriguez C, et al. Atazanavir plus ritonavir or saquinavir, and lopinavir/ritonavir in patients experiencing multiple virological failures. *AIDS.* 2005;19:685-694. **5.** REYATAZ [package insert]. Princeton, NJ: Bristol-Myers Squibb. **6.** Wolters Kluwer. SDI Product Brand Report. Total Patient Tracker; November 2010. **7.** Wolters Kluwer Pharma Solutions, Source® PHAST Prescription Monthly, November 2006-October 2011. **8.** Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. October 10, 2006; 1-122. Available at: http://www.aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL000629.pdf. Accessed February 16, 2011. **9.** Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. October 14, 2011; 1-167. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed December 1, 2011. **10.** Aptivus® (tipranavir) [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals. **11.** Crixivan® (indinavir sulfate) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc. **12.** Invirase® (saquinavir mesylate) [package insert]. Nutley, NJ: Roche Pharmaceuticals. **13.** Kaletra® (lopinavir/ritonavir) [package insert]. North Chicago, IL: Abbott Laboratories. **14.** Lexiva® (fosamprenavir calcium) [package insert]. Research Triangle Park, NC: GlaxoSmithKline. **15.** Norvir® (ritonavir) [package insert]. North Chicago, IL: Abbott Laboratories. **16.** Prezista® (darunavir) [package insert]. Raritan, NJ: Tibotec Therapeutics. **17.** Viracept® (nelfinavir mesylate) [package insert]. La Jolla, CA: Agouron Pharmaceuticals, Inc.

Please see REYATAZ Full Prescribing Information in pocket.

REYATAZ®
(atazanavir sulfate) 200 mg/300 mg capsules
UP TO THE CHALLENGE
IN HIV COMBINATION THERAPY

Please see Important Safety Information for REYATAZ on pages 14-15 and for efavirenz on card in pocket.

* As-treated population, according to the study drug received.
† Intent-to-treat, as randomized population.
‡ REYATAZ 400 mg (without ritonavir) once daily taken with food as part of combination therapy is the current dose recommendation for treatment-naive adults who are unable to tolerate ritonavir.
§ Values obtained after initiation of serum lipid-reducing agents were not included in these analyses. The change from baseline is the mean of within-patient changes from baseline and is not a simple difference of the baseline and mean values at Week 48 or 96.

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UP TO THE CHALLENGE
IN HIV COMBINATION THERAPY

Sustained virologic suppression

- CASTLE Study (96-week results): 75% of treatment-naive adults (n=441) and 74% of those with a high baseline viral load (≥100,000 copies/mL, n=223) achieved HIV-1 RNA <50 copies/mL on a REYATAZ/r-based regimen (cross-sectional analysis)*
  - Primary endpoint (48 weeks): 78% of 440 adults achieved HIV-1 RNA <50 copies/mL (CVR, NC=F)[11]
- Study 034 (48-week results): 67% (32%) of treatment-naive adults (n=405) achieved HIV-1 RNA <400 (<50) copies/mL on the REYATAZ without/r-based regimen†
- Study 045 (48-week results): Mean TAD in change of HIV-1 RNA levels from baseline of -1.58 $\log_{10}$ copies/mL in treatment-experienced adults (n=119) on a REYATAZ/r-based regimen
  - 55% (38%) achieved HIV-1 RNA <400 (<50) copies /mL
  - Virologic response with REYATAZ/r is based on both the number and type of baseline primary PI mutations

A safety/tolerability profile you expect

- Selected grade 2-4 treatment-emergent adverse reactions in CASTLE, Study 034, and Study 045, respectively:
  - Diarrhea (2%, 1%, 3%), jaundice/scleral icterus (5%, 7%, 9%), myalgia (<2%, <2%, 4%), nausea (4%, 14%, 3%), and rash (3%, 7%, <2%)
- Selected grade 3-4 lab abnormalities in CASTLE, Study 034, and Study 045, respectively:
  - AST Elevation ≥5.1 x ULN (3%, 2%, 3%), ALT Elevation ≥5.1 x ULN (3%, 4%, 4%), and total bilirubin ≥2.6 x ULN (44%, 35%, 49%)
- Low rate of discontinuation due to adverse events (3% in CASTLE, 5% in Study 034, and 4% in Study 045)[4,5]

A lipid profile that's an important consideration for you and your patients

- Mean changes§ in lipid parameters for REYATAZ/r in CASTLE (Week 96; n=342), REYATAZ without/r in Study 034 (Week 48; n=272), and REYATAZ/r in Study 045 (Week 48; n=74) were: total cholesterol, +13%, +2%, and -8%; LDL cholesterol, +14%, +1%, and -10%; HDL cholesterol, +21%, +13%, and -7%; and triglycerides, +13%, -9%, and -4%
- The clinical impact of these findings has not been demonstrated

Recommended dosing that's always once daily

- Taken with ritonavir as a single daily dose with food as part of a regimen

Experience that counts

- Over 200,000 patients treated since 2003[6]

Please see Important Safety Information for REYATAZ on pages 14-15 and for efavirenz on card in pocket.

IN AN HIV REGIMEN...
REYATAZ FIGHTS FOR YOUR PATIENTS, WITH...

REYATAZ RESOURCE

CLINICAL FINDINGS IN THE FIGHT AGAINST HIV

CASTLE Study:

Once-daily atazanavir/ritonavir versus twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1–infected patients: 48 week efficacy and safety results of the CASTLE study.
— Molina, et al. *Lancet.* 2008.[1]

Once-daily atazanavir/ritonavir compared with twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1–infected patients: 96-week efficacy and safety results of the CASTLE study.
— Molina, et al. *J Acquir Immune Defic Syndr.* 2010.[2]

Study 034:

Comparison of once-daily atazanavir with efavirenz, each in combination with fixed-dose zidovudine and lamivudine, as initial therapy for patients infected with HIV.
— Squires, et al. *J Acquir Immune Defic Syndr.* 2004.[3]

Study 045:

Atazanavir plus ritonavir or saquinavir, and lopinavir/ritonavir in patients experiencing multiple virological failures.
— Johnson, et al. *AIDS.* 2005.[4]

INDICATION: REYATAZ is indicated in combination with other antiretroviral agents for treatment of HIV-1 infection. This is based on analyses of plasma HIV-1 RNA levels and CD4+ cell counts from controlled studies of 96 weeks (treatment-naive) and 48 weeks (treatment-experienced) duration in adult and pediatric patients at least 6 years of age. The following should be considered when initiating REYATAZ:

- In Study 045, REYATAZ/ritonavir and lopinavir/ritonavir were similar for the primary efficacy measure of time-averaged difference in change from baseline in HIV RNA. This study was not large enough to reach a definitive conclusion that REYATAZ/ritonavir and lopinavir/ritonavir are equivalent on the secondary efficacy measure of proportions below the HIV RNA lower limit of detection.
- The number of baseline primary protease inhibitor mutations affects virologic response to REYATAZ/ritonavir.

Selected Important Safety Information

- **Hypersensitivity:** REYATAZ is contraindicated in patients with previously demonstrated clinically significant hypersensitivity (eg, Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to any of the product components

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IN HIV COMBINATION THERAPY

IN AN HIV REGIMEN…

REYATAZ FIGHTS FOR YOUR PATIENTS

Results from clinical trials across patient types

	CASTLE Study 96 weeks Treatment-naive (with ritonavir)	Study 034 48 weeks Treatment-naive (without ritonavir)*	Study 045 48 weeks Treatment-experienced (with ritonavir)
Sustained virologic response • Virologic response with REYATAZ/ritonavir is based on both the number and type of baseline primary mutations – Please see pages 6-7 for efficacy results	✓ 75% of 441 patients achieved and maintained HIV-1 RNA <50 copies/mL	✓ 67% of 405 patients achieved and maintained HIV-1 RNA <400 copies/mL	✓ The mean HIV-1 RNA change from baseline was -1.58 $\log_{10}$ copies/mL (n=119)†
Low incidence of diarrhea • **1-3%** moderate to severe diarrhea – Please see page 8 for Grade 2-4 adverse events	✓ 2% of 441 patients had moderate to severe diarrhea	✓ 1% of 404 patients had moderate to severe diarrhea (Median time on therapy 64 weeks)	✓ 3% of 119 patients had moderate to severe diarrhea
A lipid profile that's an important consideration for you and your patients • The clinical impact of these findings has not been demonstrated – Please see page 11 for mean lipid percentage changes	✓ (n=342) 13% increase in total cholesterol 14% increase in LDL cholesterol 21% increase in HDL cholesterol 13% increase in triglycerides	✓ (n=272) 2% increase in total cholesterol 1% increase in LDL cholesterol 13% increase in HDL cholesterol 9% decrease in triglycerides	✓ (n=74) 8% decrease in total cholesterol 10% decrease in LDL cholesterol 7% decrease in HDL cholesterol 4% decrease in triglycerides
Recommended dosing that's always once daily • Taken as a single daily dose with food – Please see page 13 for dosing recommendations	✓	✓	✓

Selected Important Safety Information

- **Drug interactions:** Coadministration with drugs highly dependent on CYP3A or UGT1A1 for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events is contraindicated. These and other contraindicated drugs are alfuzosin, rifampin, irinotecan, orally administered midazolam, triazolam, dihydroergotamine, ergotamine, ergonovine, methylergonovine, cisapride, St. John's wort (*Hypericum perforatum*)-containing products, lovastatin, simvastatin, pimozide, sildenafil dosed as Revatio®, or indinavir

* REYATAZ 400 mg (without ritonavir) once daily taken with food as part of combination therapy is the current dose recommendation for treatment-naive adults who are unable to tolerate ritonavir.
† 55% (38%) achieved HIV-1 RNA <400 (<50) copies/mL.

Please see Important Safety Information for REYATAZ on pages 14-15 and for efavirenz on card in pocket.

IMPORTANT SAFETY INFORMATION (continued)

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