**Atazanavir (Reyataz®)**

**Class:**
Atazanavir is an HIV protease inhibitor.

**Antiviral Activity:**
Atazanavir has activity against HIV-1.

**Mechanism of Action:**
Atazanavir forms an inhibitor-enzyme complex with HIV protease preventing the normal maturation process of HIV and formation of mature infectious virions.

**Mechanism of Resistance:**
Higher levels of protease inhibitor resistance result from the accumulation of multiple protease inhibitor-resistance mutations. The many mechanisms of resistance include reduced binding affinity between the inhibitor and the protease enzyme, alterations in enzyme catalysis, effects on dimer stability, alterations in inhibitor binding kinetics, and re-shaping of the active site.

**Pharmacodynamics:**
By inhibiting the HIV protease enzyme, therapy with atazanavir decreases plasma HIV-1 RNA and increases CD4+ T cell counts in HIV infected individuals. *In vitro* studies have integrated plasma concentrations with antiviral activity.

**Pharmacokinetics:**
Administration of atazanavir with food increases bioavailability and reduces intersubject variation in systemic exposure. Atazanavir is 86% bound to plasma proteins and is metabolized by CYP450 3A4 via monooxygenation and dioxygenation with subsequent glucuronidation.

**Adverse Effects:**
Hyperbilirubinemia is the most common adverse effect. Diarrhea, nausea and abdominal pain can also be seen. Atazanavir does not appear to significantly alter lipid metabolism over the short term unlike other protease inhibitors.

**Dosage:**
Capsule 100mg, 150mg, 200mg

Adolescents and adults:
Antiretroviral naïve patients – 400 mg once daily
Antiretroviral-experienced patients – 300 mg once daily in combination with ritonavir 100 mg once daily

Children: the recommended dose has not yet been established.

Disease state based dosing:
Renal Impairment: no dose adjustment necessary
Hepatic Impairment: no dose adjustment necessary but caution should be exercised.

**Contraindications/Warnings/ Precautions:**
Atazanavir is contraindicated with:
midazolam, triazolam, dihydroergotamine, ergotamine, ergonovine, methylergonovine, cisapride (no longer marketed in the United States) and pimozide.

**Drug Interactions:**
Atazanavir is a known substrate and inhibitor of CYP3A4 *in vitro*. Therefore, medications that are also metabolized by CYP3A4 may interact with atazanavir.

**Pregnancy:**
Category B: no evidence of risk in humans but studies inadequate.

**Monitoring Requirements:**
HIV-RNA, bilirubin

**Brand names/Manufacturer:**
Reyataz®/Bristol-Myers Squibb