

## **Darunavir (Prezista®) (PDF Version)**

### **Class:**

Darunavir is an HIV protease inhibitor.

### **Antiviral Activity:**

Darunavir has activity against HIV-1.

### **Mechanism of Action:**

Darunavir inhibits the HIV protease enzyme by forming an inhibitor-enzyme complex thereby preventing cleavage of the gag-pol polyproteins. Immature, non-infectious viral particles are subsequently produced.

### **Mechanism of Resistance:**

Higher levels of protease inhibitor resistance result from the accumulation of multiple protease inhibitor-resistance mutations. There are many mechanisms of resistance. These 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:**

In peripheral blood mononuclear cells without human serum, median EC50s ranged from 1 to 8.5 nM, and median EC90s ranged from 2.7 to 13nM.

### **Pharmacokinetics:**

There is a 30% increase in darunavir AUC and Cmax when taken with food compared to fasting. Darunavir is 95% protein bound to alpha-1-acid glycoprotein. Darunavir is metabolized extensively by the CYP3A subfamily of enzymes. The majority of darunavir is eliminated in the feces.

### **Adverse Effects:**

Adverse effects are diarrhea, nausea, headache, nasopharyngitis, abdominal pain, vomiting, rash, constipation, increased prothrombin time, elevated alkaline phosphatase, hypercholesterolemia, hypertriglyceridemia, elevated lipase, elevated amylase, hypernatremia and thrombocytopenia.

### **Dosage:**

Tablet 75mg, 150mg, 300mg, 400mg, 600mg

The recommended dose for antiretroviral-naïve adult patients is 800mg with 100mg ritonavir once daily administered with food. The recommended dose for antiretroviral-experienced adult patients is 600mg with 100mg ritonavir twice daily administered with food.

For children and adolescents 6 to 17 years of age, the following weight-based dosing is recommended for darunavir/ritonavir: 20-29kg 375/50mg twice daily, 30-39kg 450/60mg twice daily, and 40+kg 600/100mg twice daily.

There are currently no recommendations for use of darunavir in pediatric patients under 6 years of age.

Disease state based dosing:

Renal Impairment: no dose adjustment necessary

Hepatic Impairment: no dose adjustment but use caution in patients with hepatic Insufficiency; not recommended in patients with severe hepatic impairment.

**Contraindications/Warnings/ Precautions:**

Darunavir is contraindicated with the following medications:

dihydroergotamine, ergonovine, ergotamine, methylergonovine, cisapride, pimozide, oral midazolam, triazolam, St. Johns Wort, lovastatin, simvastatin, and rifampin.

**Drug Interactions:**

*In vitro*, darunavir has been shown to be an inhibitor of, CYP3A4. Darunavir alone can induce CYP3A4, but co-administration with ritonavir results in net inhibition of CYP3A4 activity. Therefore, any medication metabolized by CYP3A4 may interact with darunavir given with ritonavir.

**Pregnancy:**

Category C: Risk unknown. Human studies inadequate.

**Monitoring Requirements:**

Blood glucose, LFTs, serum lipid profile, pancreatic enzymes

**Brand names/Manufacturer:**

Prezista®/Tibotec Therapeutics Norvir®/Abbott Laboratories