

RILPIVIRINE (RPV) (Updated August 2011)	
Trade Name	Edurant
Classification	Non-nucleoside Reverse Transcriptase Inhibitor
Form	25-mg tablet Each Complera tablet contains FTC 200 mg, RPV 25 mg, and TDF 300 mg
Dosing Recommendations	For ART-naïve patients: one 25-mg tablet once daily with a meal (≥550 calories)
Hepatic Impairment Dosing	No dose adjustment needed for mild to moderate (Child-Pugh A and B) hepatic impairment
Renal Impairment Dosing	Use standard dose with close monitoring in patients with ESRD. RPV unlikely to be removed during hemodialysis and peritoneal dialysis
Food Effect	Normal or high-fat meal improves RPV absorption. Fasted condition or high protein drink decreases RPV absorption by 40-50%. High protein binding 99.7%
Oral Bioavailability	Absolute bioavailability unknown, but food improves absorption
Serum Half-life	50 hrs
Elimination	Metabolized via CYP3A4. Not an inducer or inhibitor of CYP450 isoenzymes. Parent drug and metabolite are primarily excreted in the feces (85%) and urine (6.1%)
Adverse Events	Less CNS side effect compared to efavirenz (e.g., depression, insomnia, headache, dizziness), rash Fat redistribution, immune reconstitution syndrome May prolong QTc interval. Rilpivirine should be used with caution when co-administered with a drug with a known risk of Torsade de Pointes Avoid rilpivirine co-administration with drugs that can significantly prolong QTc interval
FDA Pregnancy Category	B
Long-Term Animal Carcinogenicity Studies	At high concentrations in mice, rilpivirine induced hepatocellular neoplasms
Animal Teratogen Studies	Not teratogenic in animal studies. No human data
Black Box Warnings	None
Drugs to Avoid	As part of the ARV regimen: Any other NNRTIs (e.g., DLV, EFV, ETR, NVP) Carbamazepine, dexamethasone (long-term use), esomeprazole, lansoprazole, omeprazole, oxcabazepine, pantoprazole, phenobarbital, phenytoin, rifabutin, rabeprazole, rifampin, rifapentine, St John's wort

Cautious Use or Dose Adjustment	
Antiretrovirals	<p>Darunavir: DRV/r ↑ RPV AUC 130% - Use standard dose</p> <p>Didanosine: No significant interaction if ddI given 2 hours before RPV. RPV concentrations not affected</p> <p>Lopinavir/ritonavir: LPV/r ↑ RPV AUC 52% - Use standard dose</p> <p>Tenofovir: TDF AUC ↑ 23%. RPV concentrations not affected. Use standard dose</p>
Antimycobacterials	Macrolide antibiotics (e.g., clarithromycin, erythromycin, troleandomycin) may ↑ RPV concentrations. Monitor for QTc prolongation. Consider azithromycin with co-administration
Antifungals	<p>Ketoconazole: Ketoconazole ↑ RPV AUC 49%; RPV ↓ ketoconazole AUC 24%</p> <p>Azole antifungal agents may ↑ RPV concentrations. Monitor for QTc prolongation and antifungal efficacy</p>
Erectile Dysfunction Agents	Sildenafil: No significant interaction
H2 Receptor Antagonists	Use with caution. H2 blockers must be given 12 hrs before or 4 hrs after RPV. Antacids should also be administered >2 hrs before of 4 hrs after RPV
Lipid-Lowering Agents	Atorvastatin: ATO metabolites ↑ 23-39%; clinical significance unknown. Use stand dose atorvastatin
Oral Contraceptives	<p>Ethinyl estradiol: AUC ↑ 14%</p> <p>Norethindrone: AUC ↓ 11%</p> <p>Clinical significance unknown – Use additional method of contraception</p>
Synthetic Narcotics	Methadone (active R-isomer): AUC ↓ by 26%. Monitor for withdrawal symptoms
With CYP3A Inducers	Co-administration of RPV and drugs that induce CYP3A (e.g., carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifamycin antibiotic) may result in ↓ plasma concentrations of RPV and loss of virologic response and possible resistance
With CYP3A Inhibitors	Co-administration of RPV and drugs that inhibit CYP3A may result in ↑ plasma concentrations of RPV