

NEVIRAPINE (NVP) (Updated March 2011)	
Trade Name	Viramune
Classification	Non-nucleoside Reverse Transcriptase Inhibitor
Form	200-mg immediate-release tablets; 400-mg extended-release tablets; 50 mg/5 mL oral suspension
Dosing Recommendations	<p>For NVP-naïve patients: one 200-mg immediate-release tablet daily for 14 days, then one 400-mg extended-release tablet daily with or without food</p> <p>For patients transitioning from immediate-release NVP: one 400-mg extended-release tablet daily</p> <p><i>Note:</i> Patients must never take more than one form of NVP at the same time</p>
Hepatic Impairment Dosing	Should not be administered in patients with moderate to severe hepatic impairment; patients with hepatic fibrosis or cirrhosis may be at risk for drug accumulation
Food Effect	No food effect
Oral Bioavailability	>90%
Serum Half-life	25-30 hours
Elimination	Metabolized by cytochrome P450 (3A4 inducer); 80% excreted in urine (glucuronidated metabolites, <5% unchanged), 10% in feces
Adverse Events	<p>Rash,* fever, nausea, headache</p> <p>Increased transaminase levels, symptomatic hepatitis, including hepatic necrosis</p>
FDA Pregnancy Category	C (no fetal defect was found in HIVNET 006 trial)
Long-Term Animal Carcinogenicity Studies	Not completed
Animal Teratogen Studies	Negative
Black Box Warnings	<p>Severe, life-threatening, and in some cases fatal hepatotoxicity, including fulminant and cholestatic hepatitis, hepatic necrosis and hepatic failure, has been reported in patients treated with nevirapine. In some cases, patients presented with non-specific prodromal signs or symptoms of hepatitis and progressed to hepatic failure. These events are often associated with rash. Women and patients with higher CD4 counts are at increased risk of these hepatic events. Women with CD4 counts >250 cells/mm³, including pregnant women receiving chronic treatment for HIV infection, are at considerably higher risk for these events. Patients with signs or symptoms of hepatitis must discontinue nevirapine and seek medical evaluation immediately.</p> <p>Severe, life-threatening skin reactions, including fatal cases, have occurred in patients treated with nevirapine. These have included cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, and hypersensitivity reactions characterized by rash, constitutional findings, and organ dysfunction. Patients developing signs or symptoms of severe skin reactions or hypersensitivity reactions must discontinue nevirapine and seek medical evaluation immediately.</p> <p>It is essential that patients be monitored intensively during the first 18 weeks of therapy with nevirapine to detect potentially life-threatening hepatotoxicity or</p>

	skin reactions. The greatest risk of severe rash or hepatic events (often associated with rash) occurs in the first 6 weeks of therapy. However, the risk of any hepatic event, with or without rash, continues past this period, and monitoring should continue at frequent intervals. In some cases, hepatic injury has progressed despite discontinuation of treatment. Nevirapine should not be restarted following severe hepatic, skin or hypersensitivity reactions. In addition, the 14-day lead-in period with nevirapine 200 mg daily dosing must be strictly followed.
Drugs to Avoid	As part of ARV regimen: Atazanavir Other NNRTIs (e.g., ETR, EFV, and DLV) Garlic supplements, ketoconazole, rifampin, rifapentine, St. John's wort
Cautious Use or Dose Adjustment	
Antiretrovirals	Darunavir: No data. Consider DRV/r 600/100 mg twice-daily with NVP co-administration Indinavir: IDV ↓ 28% – ↑ IDV dose to 1000 mg q8h, or consider IDV 800 mg + RTV 100 mg twice daily Lopinavir/ritonavir: LPV C _{min} ↓ 55% – ↑ LPV/r dose to 500/125 mg (3 tabs or 7.5 mL) twice daily with food Maraviroc: Use maraviroc 300 mg twice daily with standard NVP dose Raltegravir: No data. Interaction unlikely. Use standard dose Saquinavir: SQV ↓ 25% – Use SQV 1000 mg + RTV 100 mg twice daily
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin: Unknown – Avoid co-administration. If no alternatives available, use with close monitoring of anticonvulsant levels
Antifungals	Fluconazole: May significantly ↑ NVP concentrations – Monitor for NVP-associated adverse effects Itraconazole: May ↓ itraconazole concentrations and ↑ NVP concentrations. Monitor itraconazole concentrations with co-administration Voriconazole: Potential for bi-directional inhibition; may significantly ↓ voriconazole and ↑ NVP concentrations – Monitor voriconazole serum concentrations and NVP toxicities
Antimycobacterials	Clarithromycin: NVP ↑ 26%; CL ↓ 31% – Monitor for efficacy or use alternative agent (azithromycin)
Oral Contraceptives	Ethinyl estradiol: EE ↓ ~20% – Use alternative or additional method of contraception Norethindrone: ↓ norethindrone – Use alternative or additional method of contraception
Synthetic Narcotics	Methadone: ↓ methadone levels significantly – Monitor and titrate dose to effect
* In clinical trials, NVP was discontinued because of rash in 7% of patients. Rare cases of Stevens-Johnson syndrome have been reported.	