Nevirapine (Viramune®, NVP)

Class:
Nevirapine is a dipyridiazepinone compound.

Antiviral Activity:
Non-nucleoside reverse transcriptase inhibitors (NNRTIs) are highly selective for HIV-1 but do not exhibit activity against other viruses.

Mechanism of Action:
NNRTIs bind noncompetitively to an active site of the reverse transcriptase molecule. Reverse transcriptase directs the polymerization of DNA from viral RNA. NNRTIs inhibit this polymerization by altering the position of critical amino acids within the catalytic site.

Mechanism of Resistance:
Resistance of NNRTIs occurs through mutations of the reverse transcriptase gene in the viral genome. When nonnucleoside reverse transcriptase inhibitors are used as monotherapy for HIV-1 infection, drug resistance develops rapidly.

NNRTI naïve patients with prior nucleoside analogue reverse transcriptase inhibitor (NRTI) exposure, who have isolates with resistance mutations and phenotypic resistance to NRTIs, appear more likely to have hypersusceptibility to the NNRTI class of drugs.

Pharmacodynamics:
*In vitro* IC₅₀ for nevirapine ranges between 0.01 and 0.1 µM.

Pharmacokinetics:
Nevirapine is well absorbed after oral administration. Its absolute bioavailability appears to be > 90% and maximum concentrations are generally achieved by 4 hours after an oral dose. It is approximately 60% bound to plasma proteins. Nevirapine is extensively metabolized by the cytochrome P450 system, mainly 3A4. Nevirapine is an inducer of CYP450 3A4, which leads to autoinduction.

Adverse Effects:
The most common adverse effects are hepatitis and rash.

Dosage:
Suspension 50mg/ml (240ml bottle)
Tablet 200mg (60 tablet bottle)

Adult dosing:
200 mg/day lead in for 2 weeks then 200 mg twice daily
Patients who interrupt nevirapine dosing for more than 7 days should restart with lead-in.
Pediatric Dosing:
2 months up to 8 years of age - 4 mg/kg once daily for the first 14 days followed by 7 mg/kg twice daily thereafter.
8 years and older - 4 mg/kg once daily followed by 4 mg/kg twice daily thereafter
(Total nevirapine dose should not exceed 400mg)

Disease state based dosing:
No dose adjustment is necessary for mild to severe renal insufficiency. Patients on dialysis should receive an additional 200mg dose after each dialysis.

There are no significant changes in the pharmacokinetics of nevirapine with mild or moderate hepatic impairment. Nevirapine should not be given to patients with severe hepatic impairment.

Contraindications/Warnings/Precautions:
Severe, life threatening, and in some cases fatal hepatotoxicity, including fulminant and cholestatic hepatitis, hepatic necrosis and hepatic failure and severe, life threatening skin reactions have been reported with the use of nevirapine.

Drug Interactions:
Nevirapine is an inducer of hepatic cytochrome P450 3A. Therefore medications that are metabolized by CYP3A may interact with nevirapine.

Pregnancy:
Category C: Risk unknown. Human studies inadequate.
Nevirapine is well studied and tolerated as an antiretroviral agent to prevent perinatal transmission. However, there is concern over the emergence of resistance after using nevirapine to prevent mother to child transmission.

Monitoring Requirements:
NNRTIs are suitable for TDM for several reasons, including considerable interpatient variability in concentrations among patients who take the same dose and data indicating relationships between the concentration of drug in the body, the anti-HIV effect and in some cases, toxicity.

Liver function tests should be monitored in patients taking nevirapine.

Brand names/Manufacturer:
Viramune®
Boehringer Ingelheim Pharmaceuticals Inc