Abacavir (Ziagen®, ABC)

Class:
Abacavir is a synthetic carbocyclic nucleoside.

Antiviral Activity:
In vitro activity against HIV-1 with expected activity against non-clade B HIV-1 strains and HIV-2.

Mechanism of Action:
Nucleoside Analog Reverse Transcriptase Inhibitor (NRTI) Abacavir is intracellularly phosphorylated to carbovir triphosphate, which is incorporated into the HIV DNA during reverse transcription. Carbovir triphosphate lacks a 3'-OH group and thus results in chain termination.

Mechanism of Resistance:
Resistance to NRTI's occurs through two mechanisms; decreased incorporation of NRTI into the viral DNA and increased excision of NRTI from viral DNA.

Pharmacodynamics:
The IC_{50} of abacavir against HIV-1_{IIIB} ranges from 3.7 to 5.8 µM and from 0.07 to 1.0 µM against HIV-1_{BaL}.

Pharmacokinetics:
There is rapid absorption of abacavir from oral dosage forms. Maximum concentrations of abacavir are reached in approximately 0.8 hours after dosing. Abacavir undergoes extensive (~98%) hepatic transformation via the alcohol dehydrogenase and glucuronyl transferase enzymes to inactive metabolites. Abacavir is ~50% bound to plasma proteins.

Adverse Effects:
Nausea and or vomiting, diarrhea, headache, rash, malaise, asthenia and fatigue are common if combined with zidovudine and lamivudine. Lactic acidosis has also been reported.

Dosage:
Solution - 20 mg/ml (240ml, strawberry-banana flavor)
Tablet - 300mg (60 tablet bottle and 10 x 6 blister packs)

Adults: 300mg twice daily in naive or experienced patients.

Pediatrics: A dose of 8 mg/kg twice daily (maximum daily dose of 300mg) in children between the ages of 3 months and 16 years is recommended. The use of this dose is being studied in patients under three months of age.

Disease state based dosing:
Dose adjustment is not necessary in renal impairment or in dialysis.

A dose of 200mg twice a day is recommended in patients with mild hepatic dysfunction (Child-Pugh score 5 to 6).

Contraindications/Warnings/Precautions
Fatal hypersensitivity reactions have been reported. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of NRTI's.

Drug Interactions:
Abacavir does not inhibit *in vitro* drug metabolism mediated by the CYP 450 3A4, 2D6, 2C9 or 2E1 isoenzymes of the cytochrome P450 system. Thus Drug interactions will be minimal.

Pregnancy:
Category C
Abacavir should only be used if the benefits outweigh the risk. There have been no formal studies of abacavir in pregnant women.

Monitoring Requirements:
There are no specific monitoring parameters for abacavir.

Brand names/Manufacturer:
Ziagen®
Glaxo Wellcome Division Smithkline Beecham Corp