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$_{HIV}$ 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