Tenofovir (Viread®, TDF)

Class:
Tenofovir is a nucleotide analogue.

Antiviral Activity:
Tenofovir has activity against HIV-1, including non-clade B strains, HIV-2 and hepatitis B virus.

Mechanism of Action:
Tenofovir disoproxil fumarate is hydrolyzed to tenofovir, which is then phosphorylated to tenofovir diphosphate. Tenofovir diphosphate inhibits the activity of HIV-1 reverse transcriptase by competing with the natural substrate, deoxyadenosine 5'-triphosphate, and by DNA chain termination.

Mechanism of Resistance:
Resistance to nucleotide analogues occurs through two mechanisms; decreased incorporation of the nucleotide analogue into the viral DNA and increased excision of the nucleotide from the viral DNA.

Pharmacodynamics:
In two phase I randomized, double blind, placebo-controlled trials, a dose-proportional increase in drug exposure was associated with incremental decreases of plasma HIV-1 RNA (viral load). The maximum effect was seen at an oral dose of 300 mg once daily. The antiviral effect of tenofovir may persist following drug discontinuation.

Pharmacokinetics:
The oral bioavailability of a 300 mg dose of TDF is 25% in the fasted state. Administration with high fat meal increases tenofovir AUC and C_{max} by 40% and 14%, respectively. Protein binding *in vitro* is less than 7%. It is not appreciably metabolized by the liver and the renal route is the primary elimination pathway.

Adverse Effects:
Adverse effects include nausea, vomiting, diarrhea, asthenia, headache, flatulence, abdominal pain and anorexia.

Dosage:
Tablet 300mg

Adults and Adolescents:
300 mg orally once daily with a meal
Children: dose has not been established

Disease state based dosing:
Renal Impairment:
CrCl 30-49 ml/min – 300 mg every 48 hours

CrCl 10-29 ml/min – 300 mg twice per week
Hemodialysis – 300 mg every 7 days OR 300mg following a total of approximately 12 hours of dialysis
Hepatic Impairment:
No dose adjustment necessary

Contraindications/Warnings/ Precautions:
Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleotide analogues.

Drug Interactions:
Tenofovir slightly inhibits CYP1A2. However, this is not expected to lead to any clinically significant drug interactions.

Pregnancy:
Category B: No evidence of risk in humans but studies inadequate.

Monitoring Requirements:
LFTs, baseline serum creatinine/BUN, serum phosphate

Brand names/Manufacturer:
Viread®/Gilead Sciences Inc