Stavudine (Zerit®, d4T)

Class:
Stavudine is a thymidine analogue.

Mechanism of Action:
Nucleoside reverse transcriptase inhibitor (NRTI).
Stavudine is converted to stavudine 5'-triphosphate which competes with thymidine 5'-triphosphate for incorporation into viral DNA. Stavudine 5'-triphosphate lacks a 3'-hydroxyl group and leads to chain termination.

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

Pharmacokinetics:
Stavudine bioavailability is 99% in adults and 78% in children. The volume of distribution ranges from 0.54 to 0.69 L/kg in adults and is 9.3 L/mm³ in children. Approximately 40% of a dose of stavudine can be recovered as parent drug in the urine.

Adverse Effects:
The most common adverse effect is peripheral neuropathy. Bone marrow suppression may also occur.

Dosage:
Capsule 15mg, 20mg, 30mg, 40mg
Powder for Oral Solution 1mg/ml

Adults:
= 60kg – 40 mg twice daily
< 60kg – 30 mg twice daily
Pediatric:
2 mg/kg/day in two divided doses

Disease state based dosing:
Renal Impairment:
= 60kg:
CrCl > 50ml/min – 40mg twice daily
CrCl 26-50ml/min – 20mg twice daily
CrCl 10-25ml/min – 20mg once daily
CrCl < 10ml/min – 20mg every other day
Hemodialysis – 20mg once daily after hemodialysis
< 60mg:
CrCl > 50ml/min – 30mg twice daily
CrCl 26-50ml/min – 15mg twice daily
CrCl 10-25ml/min – 15mg once daily
CrCl < 10ml/min – 15mg every other day
Hemodialysis – 15mg once daily after hemodialysis

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 NRTIs. Fatal and nonfatal pancreatitis has occurred during therapy with stavudine.

**Drug Interactions:**
Stavudine should not be administered with zidovudine due to antagonism.

**Pregnancy:**
Category C: Risk unknown. Human studies inadequate.

**Monitoring Requirements:**
CBC with differential, LFTs, platelet count, serum amylase, serum creatinine, serum lipase

**Brand names/Manufacturer:**
Zerit®/ER Squibb and Sons Inc