

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

< 60kg:

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