

Zerit (stavudine)



Zerit is supplied in 15 mg, 20 mg, 30 mg and 40 mg capsules, and as an oral solution. A new, extended-release formulation, "Zerit XR," can be taken just once per day. The regular 40-mg capsule (shown) is dark orange and imprinted with "BMS 1967" and "40" on one side. Dosing may vary.



Also known as: d4T

Background and description. Cleared for marketing by the US Food and Drug Administration (FDA) in June 1994, stavudine became the fourth agent available for the treatment of HIV infection and the second antiretroviral released under accelerated approval. Zerit is a nucleoside reverse transcriptase inhibitor (NRTI). Zerit is indicated in combination with other antiretrovirals for the treatment of HIV infection. Zerit XR is a new once-daily version that was approved by the FDA in late 2002, but has not been brought to market and therefore is **not available**. Bristol-Myers Squibb is the drug's manufacturer.

Dose. The dose of Zerit is weight-dependent. For patients weighing 132 lb or more, the recommended dose is one 40 mg capsule every 12 hours. For patients weighing less than 132 lb, the recommended dose is one 30 mg capsule every 12 hours. **For Zerit XR, a 100-mg capsule once a day is recommended for patients who weigh at least 160 lb, while a 75-mg capsule is recommended for patients who weigh less than 160 lb.**

Food restrictions. None.

Storage. Zerit capsules should be stored in a closed container and kept at a temperature of 59° to 86°F.

Patient assistance. Bristol-Myers Squibb provides a patient assistance program for those who qualify. For more information, call 800.272.4878.

Side effects and toxicity. Peripheral neuropathy is the toxicity most commonly produced by Zerit; the neuropathy is dose-related and occurs more often in patients with advanced HIV disease. Drug-related neuropathy usually resolves (although not necessarily completely) when Zerit is promptly discontinued, although the symptoms may worsen temporarily when the drug is stopped.

Elevated liver function tests are common with Zerit therapy, with clinically significant increases occurring in approximately 12% of those taking the drug. As a class, NRTIs have been implicated in damage to mitochondrial DNA and may therefore play a role in the development of metabolic and morphologic abnormalities.

Although rare, life-threatening lactic acidosis has also been associated with the use of NRTIs. In particular, Zerit and Videx are not recommended for use in pregnant women because of a potentially increased risk of lactic acidosis and liver damage.

Drug interactions. Zerit and Retrovir should not be combined since there is potential antagonism. Because additive neurotoxicity is possible, Zerit should not be combined with Hivid, and is generally *not recommended with Videx*.

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Additional info:

Resistance and cross-resistance. Mutations at positions 69, 75, and 151 are associated with resistance to stavudine; however, phenotypic resistance is slow to emerge and a consistent genotypic correlate has not been identified. The mutation at position 151 is associated with resistance to the entire NRTI class. The insertion at position 69 can also lead to broad NRTI resistance. Mutants resistant to Retrovir often retain susceptibility to Zerit. Retrovir resistance mutations have been shown to occur in antiretroviral-naive patients assigned to Zerit/Videx therapy, although this resistance has not been substantiated phenotypically.

Clinical data. START 1 compared a regimen of Zerit/Epivir/Crixivan to a regimen of Retrovir/Epivir/Crixivan in treatment-naive patients. Both combinations produced similar increases in CD4 T cell count and reductions in viral load through 48 weeks. Data from other studies indicate that Zerit alone reduces viral load by approximately 0.8 log and several trials have included it in 3-drug combinations that are effective in suppressing viral load.

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