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Stavudine *(Zerit)*

Table of Contents

Drug Summary

Stavudine, an early nucleoside reverse transcriptase inhibitor (NRTI), was used as part of combination antiretroviral therapy for years, but now has become obsolete and replaced by better-tolerated and safer options. Stavudine poses risk of serious toxicity, including peripheral neuropathy (which can be permanent), pancreatitis, lipoatrophy, and lactic acidosis. Fatal and nonfatal cases of pancreatitis and lactic acidosis have been reported, especially when stavudine was combined with didanosine. According to the Adult and Adolescent ARV Guidelines, stavudine is no longer recommended for the treatment of HIV infection due to potential severe toxicity. Further, all persons currently taking stavudine should be strongly encouraged to switch to a safer medication. The sale and distribution of all strengths of stavudine will be discontinued and removed from the market in the United States in 2020.

Key Clinical Trials

Stavudine was studied for treatment-naïve patients as part of triple therapy, such as with lamivudine plus indinavir [START I], lamivudine plus lopinavir-ritonavir [M98-863], and lamivudine plus efavirenz [DART II]. Several studies demonstrated benefits of switching stavudine to newer NRTI agents, such as tenofovir disoproxil fumarate; the switch led to decreased rates of metabolic complications and mitochondrial toxicity [903E, SNAP, and ACTG 5142].

Adverse Effects

Stavudine may cause serious adverse events and there is an FDA black box warning for lactic acidosis, hepatomegaly with steatosis, and pancreatitis. All of these reactions can be fatal. These serious adverse effects are more likely to occur if stavudine is combined with didanosine, but can occur with stavudine alone.

Stavudine can also cause peripheral neuropathy and lipoatrophy; these may not resolve with cessation of the drug.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **stavudine** is listed as Not Recommended for Initial ART in Pregnancy (due to toxicity).

- For additional information regarding the safety and toxicity of stavudine in pregnancy see the HHS Perinatal Guidelines summary on Stavudine.

Resistance

For a listing of the most common clinically significant mutations associated with stavudine (d4T) resistance, see the NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database.

Key Drug Interactions

For complete information on stavudine-related drug interactions, see the Drug Interactions section in the Stavudine (*Zerit*) Prescribing Information.