Zalcitabine (HIVID, ddC)

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Zalcitabine is classified as FDA pregnancy category C and is no longer available in the United States.

Animal Studies

Carcinogenicity

High doses of zalcitabine (more than 1,000 times that of human therapeutic exposure) have been associated with the development of thymic lymphomas in rodents.

Reproduction/Fertility

No effect of zalcitabine on reproduction or fertility in rodents has been seen. However, there is a dose-related cytotoxic effect on preimplantation mouse embryos, with inhibition at a zalcitabine concentration of 100 μM; no inhibition of postblastocyst development was observed.[1]

Teratogenicity/Adverse Pregnancy Outcomes

Teratogenicity (hydrocephalus) occurred in rats given very high doses (more than 1,000 times the maximally recommended human exposure) of zalcitabine.

Developmental toxicity, consisting of decreased fetal weight and skeletal defects, has been seen in rodents at moderate to high zalcitabine doses. Cytotoxic effects were observed on rat fetal thymocytes at zalcitabine concentrations as low as 10 μM (approximately 100 times human therapeutic exposure).

Placental and Breast Milk Passage

In primate and placental perfusion studies, zalcitabine crosses the placenta (fetal-to-maternal drug ratio approximately 0.50 to 0.60).[2] In rodents, zalcitabine concentrates in the fetal kidney and a relatively small proportion (approximately 20%) reaches the fetal brain. It is unknown if zalcitabine is excreted in breast milk.

Human Studies in Pregnancy

No studies of zalcitabine have been conducted in pregnant women or neonates.

References

1. Toltzis P, Mourton T and Magnuson T. Comparative embryonic cytotoxicity of antiretroviral nucleosides. *J Infect Dis*, 1994. 169(5):1100-2.

2. Sandberg JA, Binienda Z, Lipe G, et al. Placental transfer and fetal disposition of 2',3'-dideoxycytidine and 2',3'-dideoxyinosine in the rhesus monkey. *Drug Metab Dispos*, 1995. 23(8):881-4.