

Hivid (zalcitabine)



Hivid is supplied in 0.750 mg tablets (shown) that are oval, gray, film-coated and imprinted with "HIVID 0.750" on one side and "Roche" on the other side. The drug is also supplied in 0.375 mg tablets that are oval, beige, film-coated and imprinted with "HIVID 0.375" on one side and "Roche" on the other side.



Also known as: ddC

Background and description. When Hivid received marketing clearance from the US Food and Drug Administration (FDA) in June 1992, it became the first antiretroviral drug licensed under the accelerated approval process. The drug is produced by Hoffmann-LaRoche. Hivid is a nucleoside reverse transcriptase inhibitor (NRTI). The drug is indicated in combination with other antiretrovirals for the treatment of HIV infection.

Please note: The maker of the drug has recently announced that Hivid will no longer be available as an HIV medication after 2005.

Dose. The recommended dose is one 0.750 mg tablet every 8 hours.

Food restrictions. Hivid may be taken with or without food.

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

Patient assistance. Hoffmann-LaRoche provides a patient assistance program. For more information, call 800.282.7780.

Side effects and toxicity. Peripheral neuropathy is the toxicity most commonly produced by Hivid, occurring in approximately

one third of those receiving the drug. The risk of neuropathy is higher in individuals with advanced HIV disease, and the pain can be so severe as to require narcotic analgesics. Prompt discontinuation of the drug usually yields a slow resolution of neuropathy, but in some cases the condition is irreversible. Fatal pancreatitis has occurred in approximately 1% of those receiving Hivid.

Other toxicities reported in conjunction with Hivid use include lactic acidosis, hepatic failure, oral ulcers, esophageal ulcers and congestive heart failure. 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. **Unless faced with a pressing need for rescue therapy, HIV-infected individuals are probably best served by avoiding this drug.**

Drug interactions. Hivid should not be used with other agents that can cause peripheral neuropathy or pancreatitis, including Videx, Zerit, Emtriva, and Epivir. Since Hivid is eliminated through the kidneys, dose adjustment is required in individuals with impaired renal function. Caution should be used if combining with Viread (also eliminated through the kidneys). When administered concomitantly with Benemid (probenecid) or Tagamet (cimetidine), monitor for renal toxicity. Avoid co-administration of Maalox and Hivid.

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Additional info:

Resistance and cross-resistance. Mutations at positions 65, 69, 74 and 151 are associated with resistance to Hivid; however, resistance is slow to emerge. 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. In the Delta 1 study, no mutations were identified after 112 weeks among subjects receiving Hivid and Retrovir. Prior therapy with Efavirenz may confer cross-resistance to Hivid .

Clinical data. Although Hivid has been studied in trials involving more than 21,000 participants, the data from those trials are largely meaningless in the present-day context of highly active anti-retroviral therapy (HAART). Most of the 20 studies of Hivid examined combinations of dual NRTI therapy rarely prescribed today and only a few of the trials provided any data on Hivid's antiviral activity as measured by reductions in viral load. These limitations reflect the clinical standards and lack of technology at the time Hivid was approved.

ACTG 175 found that a combination of Hivid plus Retrovir offered improved clinical outcome when compared to Retrovir alone in antiretroviral-naive subjects. However, the combination of Hivid/Retrovir was no better than Videx alone. For study participants with a history of Retrovir use, the combination of Hivid/Retrovir offered no clinical benefit compared to continued Retrovir monotherapy. Two other trials, ACTG 229 and ACTG 193A, showed benefit in combining Hivid and a protease inhibitor.

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