

## **Zalcitabine (Hivid®, ddC)**

### **Class:**

Zalcitabine is a thymidine analog.

### **Antiviral Activity:**

Zalcitabine appears to be more active against acutely infected cells as compared to chronically infected cells.

### **Mechanism of Action:**

Nucleoside Reverse Transcriptase Inhibitor (NRTI).

The triphosphate form of zalcitabine inhibits HIV reverse transcriptase by competing for incorporation into viral DNA as well as chain termination of the viral DNA due to the lack of a 3'-OH group.

### **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.

### **Pharmacodynamics:**

*In vitro* IC<sub>50</sub> values range from 30 to 500 nM and IC<sub>95</sub> values ranged from 100 to 1000 nM.

### **Pharmacokinetics:**

The bioavailability after oral administration as a tablet or oral solution is 70-80%. It takes about 1 to 2 hours to reach maximum plasma concentrations. Approximately 75% of a dose is recovered unchanged in the urine.

### **Adverse Effects:**

Painful sensorimotor peripheral neuropathy, mainly in the lower extremities, is the dose limiting toxicity. Other common side effects include gastrointestinal complaints, allergic reactions, anemia and neutropenia. Rare cases of hepatitis, heart failure, glucose abnormalities and pancreatitis have been described.

### **Dosage:**

0.375mg tablet (100 tablet bottle)

0.75mg tablet (100 tablet bottle)

0.75mg orally every 8 hours

Disease state based dosing:

Impaired renal function:

Creatinine clearance 10 to 40 mL/min: 0.75mg every 12 hours

Creatinine clearance <10 mL/min: 0.75mg every 24 hours

#### Peripheral neuropathy

Stop if patient develops moderate symptoms, reintroduce only if symptoms improve to mild:

Reintroduce at – 0.375mg every 8 hours

#### **Contraindications/Warnings/Precautions**

Peripheral neuropathy is the major clinical adverse effect associated with zalcitabine. Symptoms may continue to progress even after discontinuation of the medication. Pancreatitis is a rare but serious adverse effect. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of NRTIs.

#### **Drug Interactions:**

Amphotericin B, foscarnet, and parenteral aminoglycosides may interfere with renal clearance of zalcitabine. Lamivudine inhibits intracellular phosphorylation of zalcitabine. Additive peripheral neuropathy has been seen with coadministration of zalcitabine with didanosine and stavudine. Probenecid and cimetidine inhibit the renal tubular secretion of zalcitabine. Aluminum and magnesium-containing antacids decrease the absorption of zalcitabine.

#### **Pregnancy:**

Category C: Risk unknown. Human studies inadequate.

Zalcitabine has been shown to be teratogenic in rats at concentrations 1365 and 2730 times above the maximum recommended human dose.

#### **Monitoring Requirements:**

Renal function, liver function, CBC, serum amylase, triglycerides and calcium.

#### **Brand names/Manufacturer:**

Hivid®

Hoffmann La Roche Inc