Cidofovir is a white crystalline powder with an aqueous solubility of \(\text{OC H P (OH)}_2\) • 2H O. It is 1-[(S)-3-hydroxy-2-(phosphonomethoxy)propyl]cytosine dihydrate (HPMPC), with beta, and gamma 1, 2, 3. Incorporation of cidofovir into the growing viral DNA chain has been associated with the development of resistant isolates following VISTIDE administration to patients. Susceptibility of the development of resistant isolates ranged from 7-15 µM. In vitro, cidofovir concentration was reduced to a level consistent with creatinine clearance, suggesting that probenecid concentration range 0.25 to 25 µg/mL. CSF concentrations of cidofovir follow- after one hr infusions of 1.0 (n = 5), 3.0 (n = 10), 5.0 (n = 2) mg/kg (See Table 2). Approximately 70 to 85% of the VISTIDE dose increases the bioavailability of cidofovir concentration range 0.25 to 25 µg/mL. CSF concentrations of cidofovir follow-

<table>
<thead>
<tr>
<th>Cidofovir Pharmacokinetic Parameters Following 3.0 and 5.0 mg/kg</th>
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<tbody>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 18)</td>
</tr>
<tr>
<td>Cmax (end of infusion)</td>
<td>7.3 ± 1.4</td>
<td>11.5</td>
</tr>
<tr>
<td>AUC (µg•hr/mL)</td>
<td>20.0 ± 2.3</td>
<td>28.3</td>
</tr>
</tbody>
</table>

**Table 2. Cidofovir Pharmacokinetic Parameters Following 3.0 and 5.0 mg/kg**

In a 26-week intravenous toxicology study in which rats received 0.6, 3, or 15 mg/kg/week (equivalent to 0.09 times the recommended human dose based on AUC 0-24h) of VISTIDE, there was evidence of renal injury and renal wasting syndrome (including Fanconi’s syndrome) have been reported. Renal function that did not return to base- line was noted in 11% of rats treated with VISTIDE. Cidofovir and the rate of appearance of cidofovir in the urine was increased in a concentration-dependent manner. The renal clearance of cidofovir was greater than creatinine clearance, indicating that renal clearance is the major route of elimination. The pharmacokinetics of cidofovir administered as a single dose were similar to those of multiple doses, as there were no appreciable differences noted in the overall pattern of plasma cidofovir concentration versus time profiles. The renal clearance of cidofovir was determined from plasma cidofovir concentrations using urinary cidofovir recoveries.

**Mechanism of Action:**

Cidofovir is a purine nucleoside analog that inhibits viral DNA synthesis. Cidofovir is a potent inhibitor of CMV replication and is active in vitro against a variety of laboratory and clini- cally relevant isolates. Cidofovir suppresses CMV replication by selectively inhibiting the viral DNA polymerase and DNA ligase of the CMV DNA replication complex. Cidofovir is active in vitro at concentrations of \(\geq 0.25 \mu M\) to \(\geq 25 \mu M\). Cidofovir has been shown to be active in vitro at concentrations of \(\geq 0.25 \mu M\) to \(\geq 25 \mu M\) against a variety of laboratory and clini- cally relevant isolates. Cidofovir suppresses CMV replication by selectively inhibiting the viral DNA polymerase and DNA ligase of the CMV DNA replication complex. Cidofovir is active in vitro at concentrations of \(\geq 0.25 \mu M\) to \(\geq 25 \mu M\) against a variety of laboratory and clini- cally relevant isolates. Cidofovir suppresses CMV replication by selectively inhibiting the viral DNA polymerase and DNA ligase of the CMV DNA replication complex. Cidofovir is active in vitro at concentrations of \(\geq 0.25 \mu M\) to \(\geq 25 \mu M\) against a variety of laboratory and clini- cally relevant isolates. Cidofovir suppresses CMV replication by selectively inhibiting the viral DNA polymerase and DNA ligase of the CMV DNA replication complex.
Probenecid must be administered orally with each VISTIDE dose. Two

Pediatric Use

avoid postnatal transmission of HIV to a child who may not yet be infected.

It is not known whether cidofovir is excreted in human milk. Since many drugs are

1. Metabolism: Radio labelling, metabolised by 3-5% as parent, 15% as cidofovir (diphosphate), 31% as cidofovir (triphosphate) and 4% as unidentifiable metabolites. The mean plasma clearance is 0.16 L/h and the plasma half-life is 9.6 hours. More than 80% of the dose is excreted in the urine as unchanged drug. Less than 10% of the dose is excreted in the feces. After a single 5 mg/kg dose in adult volunteers, plasma concentrations peaked at 24 h and were undetectable after 96 h. Based on these data, cidofovir was administered every other week to patients with CMV retinitis (Study 106) and every week to patients with CMV esophagitis (Study 107).

2. Ingestion of food prior to each dose of probenecid may reduce drug-related nausea and vomiting.

3. Intraocular pressure, visual acuity and ocular symptoms should be monitored for at least 6 months after discontinuation of therapy.</p>


