

Vistide®
(sidovir injection)

**For Intravenous Use Only**

**WARNING**

**Renal Impairment is the Major Target of Therapy.** Cases of acute renal failure, nephrotoxicity, and/or renal impairment may occur. Administration of VISTIDE® should be avoided in patients with moderate to severe renal impairment. If VISTIDE® treatment is necessary in patients with renal impairment, cautious use of VISTIDE® is recommended. The risk of nephrotoxicity increases with the concomitant use of other nephrotoxic agents (see DOSAGE AND ADMINISTRATION). Do not use in patients with active or untreated systemic fungal infections (see DOSAGE AND ADMINISTRATION). Do not use in patients with active or untreated fungal infections (see DOSAGE AND ADMINISTRATION).

**INTERACTIONS**

VISTIDE is contraindicated in patients with active or untreated fungal infections (see DOSAGE AND ADMINISTRATION). Do not use in patients with active or untreated fungal infections (see DOSAGE AND ADMINISTRATION).

**CONTRAINDICATIONS**

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**SIDE EFFECTS**

**Geriatric/Gender/Race**

**Cross Resistance**

Ganciclovir-resistant isolates selected in vitro following exposure to increasing concentrations of ganciclovir were cross resistant to foscarnet. Cross resistance was seen in vitro and in vivo. Cross resistance to ganciclovir was seen in vivo.

**SPECIAL POPULATIONS**

**NEWBORNs**

**Residence**

DMO isolates with reduced susceptibility to cidofovir have been selected in vitro or in vivo by the concomitant use of other nephrotoxic agents. Concomitant use of these agents increases the risk of nephrotoxicity. In patients with renal impairment, cautious use of VISTIDE® is recommended. Do not use in patients with active or untreated fungal infections (see DOSAGE AND ADMINISTRATION). Do not use in patients with active or untreated fungal infections (see DOSAGE AND ADMINISTRATION).

**CONCLUSION**

The in vitro activity of cidofovir against CMV and other herpesviruses (Table 1) has been confirmed in clinical studies of efficacy in CMV nephropathy, CMV retinitis, CMV esophagitis, CMV otitis, and CMV pneumonitis. Controlled clinical studies of efficacy have been limited to CMV retinitis. Controlled clinical studies of efficacy have been limited to CMV retinitis.

**IMPAIRMENT OF FERTILITY**

IN ANIMAL STUDIES CIDOFOVIR WAS CARCINOGENIC, TERATOGENIC AND REPRODUCTIVE TOXICANT IN MALES AND FEMALES OF BOTH SPECIES. IN A 2-YEAR CARCINOGENESIS STUDY IN MICE AT 25, 50, AND 100 mg/kg per day, CIDOFOVIR induced hyperplastic renal tubular lesions, red blood cell and white blood cell leukemia, and thyroid hyperplasia in both males and females. In a 2-year carcinogenesis study in rats, CIDOFOVIR induced hyperplastic renal tubular lesions, hyperplastic eccrine glandular lesions in male rats and thyroid hyperplasia in both males and females. At these doses, CIDOFOVIR also induced a significantly increased incidence of Zymbal's gland tumors in male rats.

**No Progression at Study Completion**

Withdrew Consent 3, 1

Discontinued Due to Adverse Event 6, 0

Median CD4 Cell Count 6, 9

Baseline Characteristics

1. Table 3: Characteristics of Patients and Clinically Important Events

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 count</td>
<td>174</td>
<td>0.01</td>
</tr>
<tr>
<td>CD8 count</td>
<td>1,072</td>
<td>0.01</td>
</tr>
<tr>
<td>Baseline</td>
<td>24.5</td>
<td>0.01</td>
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**Clinical Information**

**Geriatric/Gender/Race**

**Cross Resistance**

Ganciclovir-resistant isolates selected in vitro following exposure to increasing concentrations of ganciclovir were cross resistant to foscarnet. Cross resistance was seen in vitro and in vivo. Cross resistance to ganciclovir was seen in vivo.

**NEWBORNs**

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with AIDS warrants extreme caution due to the risk of long-term carcinogenicity and
Nursing Mothers
in rabbits at 1.0 mg/kg/day, doses which were also maternally toxic, following daily
behavior, sexual maturation or reproductive capacity in the offspring.

Granulocyte colony stimulating factor (GCSF) was used in 39% of patients.
Nephrotoxicity:

• Among the subset of patients receiving VISTIDE (cidofovir injection), 75 mg/mL for intravenous infusion, is supplied as a

Method of Preparation and Administration

VISTIDE is supplied in single-use vials. Partially used vials should be discarded (see

REFERENCES

Intracellular Metabolism of the Antiherpesvirus Agent (S)-1-[3-hydroxy-2-(

Table 4. All Clinical Adverse Events, Laboratory Abnormalities or Intervention Reactions Occurring in ≥5% of Patients

Table 5. All Clinical Adverse Events, Laboratory Abnormalities or Intervention Reactions Occurring in ≥5% of Patients

Dosage and Administration

Two cases of cutaneous adverse reactions have been reported. These involved patients with severe renal dysfunction and/or infection with one patient having received VISTIDE and one not. In both cases, the reactions were mild to moderate in severity and well-controlled with systemic corticosteroids.

Infection

• Patients receiving ≤2 mg/kg dosing is <14 days in length.

Adverse Reactions

Nephropathy, urethritis, urinary casts, urinary incontinence, urinary retention, urinary

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Applicability

 rely on the mutagenic properties of cidofovir, adequate precautions including the use of

The following additional list of adverse events/intercurrent illnesses have been observed

Decreased Platelets

Immunological system is responsible for the adaptive resistance of the host to antigens. The adaptive immune system (see Section 4.10) is

Among the subset of patients receiving VISTIDE (cidofovir injection), 75 mg/mL for intravenous infusion, is supplied as a

The maintenance dose of VISTIDE must be reduced from 5 mg/kg to 3 mg/kg for an

The recommended maintenance dose of VISTIDE in patients with a serum creatinine

On the basis of the early and efficacy of VISTIDE in patients over the age of 65 has been

In Toxicology, 8.5 mg/kg/day in older rabbits, which was also maternally toxic, and

Serum bicarbonate: ≤18 mEq/L, a calculated creatinine clearance ≤55 mL/min, and a urine protein concentration ≥1.5 g/L.

In children: ≤1.5 mg/dL, a calculated creatinine clearance ≤55 mL/min, and a urine protein concentration ≥1.5 g/L.

Allergic response to the intact protein (phosphonylmethoxy)propyl]cytosine.

In Toxicology, 8.5 mg/kg/day in older rabbits, which was also maternally toxic, and

The most frequently reported adverse events regardless of relationship to study drug

The incidence of adverse reactions reported as serious in three clinical controlled studies with VISTIDE, regardless of presumed mechanism is illustrated in Table 4.

Fever 19 (14)

Occurring in >5% of Patients

Diarrhea 30 (26)

Headache 34 (30)

Gastrointestinal System

reduction of 0.8 mg/kg/day, dosing as an 80 mg/kg bolus over 30 min, followed by a
dose of 80 mg/kg/day (administered over 30 min) for 5 consecutive days. An 80 mg/kg

doses which were also maternally toxic, following daily

Due to the mutagenic properties of cidofovir, adequate precautions including the use of

Serum aspartate aminotransferase to AST >500 U/L (≥450 U/L in ≤18 years of age), or decreased serum alanine aminotransferase to ALT >500 U/L (≥150 U/L in ≤18 years of age), or decreased serum alkaline phosphatase to ALP >500 U/L, or decreased serum bilirubin to AST >15 mg/dL, or decreased creatinine clearance to ≤15 mL/min/1.73 m².

Hepatic dysfunction has been observed in patients receiving VISTIDE and was

severe renal dysfunction and/or infection with one patient having received VISTIDE and one not. In both cases, the reactions were mild to moderate in severity and well-controlled with systemic corticosteroids.

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Dehydration

• Patients receiving ≤2 mg/kg dosing is <14 days in length.

Creatinine ≤0.2 mg/dL, or decreased creatinine clearance to ≤55 mL/min.

Consequences of chronic infection include death, development of Kaposi’s sarcoma,

Serious Adverse Events

serious renal dysfunction and/or infection with one patient having received VISTIDE and one not. In both cases, the reactions were mild to moderate in severity and well-controlled with systemic corticosteroids.

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2. Cherrington JM, Allen SJW, McKee BH, and Chen MS. Kinetic Analysis of

Dosing Regimen and Frequency, if the Entire VISTIDE dose is administered on the same day, treatment duration is

Contraindications

Nephrotoxicity:

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Older patients receiving VISTIDE (cidofovir injection) who experience adverse

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1. Factor XIII deficiency

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