Skip to main content

Cidofovir (Vistide)

??? ??????: 30 ??????/?????? 2017

1. ***Nephrotoxicity:*** Renal toxicity, as manifested by ? 2+ proteinuria, serum creati-nine elevations of ? 0.4 mg/dL, or decreased creatinine clearance ? 55 mL/min, occurred in 79 of 135 (59%) patients receiving VISTIDE (cidofovir) at a maintenance dose of 5 mg/kg every other week. Maintenance dose reductions from 5 mg/kg to 3 mg/kg due to proteinuria or serum creatinine elevations were made in 12 of 41 (29%) patients who had not received prior therapy for CMV retinitis (Study 106) and in 19 of 74 (26%) patients who had received prior therapy for CMV retinitis (Study 107). Prior foscarnet use has been associated with an increased risk of nephrotoxicity; therefore, such patients must be monitored closely (see **CONTRAINDICATIONS,**).**WARNINGS, DOSAGE AND ADMINISTRATION**
2. ***Neutropenia:*** In clinical trials, at the 5 mg/kg maintenance dose, a decrease in absolute neutrophil count to ? 500 cells/mm[3] occurred in 24% of patients. Granulocyte colony stimulating factor (GCSF) was used in 39% of patients.
3. ***Decreased Intraocular Pressure/Ocular Hypotony:*** Among the subset of patients monitored for intraocular pressure changes, a ? 50% decrease from baseline intraocular pressure was reported in 17 of 70 (24%) patients at the 5 mg/kg maintenance dose. Severe hypotony (intraocular pressure of 0-1 mm Hg) has been reported in 3 patients. Risk of ocular hypotony may be increased in patients with preexisting diabetes mellitus.
4. ***Anterior Uveitis/Iritis:*** Uveitis or iritis has been reported in clinical trials and during postmarketing in patients receiving VISTIDE (cidofovir) therapy. Uveitis or iritis was reported in 15 of 135 (11%) patients receiving 5 mg/kg maintenance dosing. Treatment with topical corticosteroids with or without topical cycloplegic agents may be considered. Patients should be monitored for signs and symptoms of uveitis/iritis during VISTIDE (cidofovir) therapy.
5. ***Metabolic Acidosis:*** A diagnosis of Fanconi's syndrome, as manifested by multiple abnormalities of proximal renal tubular function, was reported in 1% of patients. Decreases in serum bicarbonate to ? 16 mEq/L occurred in 16% of cidofovir-treated patients. Cases of metabolic acidosis in association with liver dysfunction and pancreatitis resulting in death have been reported in patients receiving VISTIDE (cidofovir) .

In clinical trials, VISTIDE (cidofovir) was withdrawn due to adverse events in 39% of patients treated with 5 mg/kg every other week as maintenance therapy.

The incidence of adverse reactions reported as serious in three controlled clinical studies in patients with CMV retinitis, regardless of presumed relationship to drug, is listed in Table 4.

Table 4. Serious Clinical Adverse Events or Laboratory Abnormalities Occurring in > 5% of Patients

[a]N =135 # patients (%)	
68 (50)	Proteinuria (? 100 mg/dL)
33 (24)	Neutropenia (? 500 cells/mm[3])
17 (24)	[b]Decreased Intraocular Pressure
21 (16)	Decreased Serum Bicarbonate (? 16 mEq/L)
19 (14)	Fever
16 (12)	Infection
16 (12)	Creatinine Elevation (? 2.0 mg/dL)
12 (9)	Pneumonia
11 (8)	Dyspnea
10 (7)	Nausea with Vomiting

[a] Patients receiving 5 mg/kg maintenance regimen in Studies 105, 106 and 107.
[b] Defined as decreased intraocular pressure (IOP) to ? 50% that at baseline. Based on 70 patients receiving 5 mg/kg maintenance dosing (Studies 105, 106 and 107), for whom baseline and follow-up IOP determinations were recorded.

The most frequently reported adverse events regardless of relationship to study drugs (cidofovir or probenecid) or severity are shown in Table 5.

The following additional list of adverse events/intercurrent illnesses have been observed in clinical studies of VISTIDE (cidofovir) and are listed below regardless of causal relationship to VISTIDE (cidofovir) . Evaluation of these reports was difficult because of the diverse manifestations of the underlying disease and because

most patients received numerous concomitant medicines.

abdominal pain, accidental injury, AIDS, allergic reaction, back pain, catheter blocked, cellulitis, chest pain, chills and fever, cryptococcosis, cyst, ***Body as a Whole:*** death, face edema, flu-like syndrome, hypothermia, injection site reaction, malaise, mucous membrane disorder, neck pain, overdose, photosensitivity reaction, sarcoma, sepsis

cardiomyopathy, cardiovascular disorder, congestive heart failure, hypertension, hypotension, migraine, pallor, peripheral vascular ***Cardiovascular System:*** disorder, phlebitis, postural hypotension, shock, syncope, tachycardia, vascular disorder, edema

cholangitis, colitis, constipation, esophagitis, dyspepsia, dysphagia, fecal incontinence, flatulence, gastritis, gastrointestinal hemorrhage, ***Digestive System:*** gingivitis, hepatitis, hepatomegaly, hepatosplenomegaly, jaundice, abnormal liver function, liver damage, liver necrosis, melena, pancreatitis, proctitis, rectal disorder, stomatitis, aphthous stomatitis, tongue discoloration, mouth ulceration, tooth caries

adrenal cortex insufficiency***Endocrine System:***

hypochromic anemia, leukocytosis, leukopenia, lym-phadenopathy, lymphoma like reaction, pancytopenia, splenic disorder, ***Hemic & Lymphatic System:*** splenomegaly, thrombocytopenia, thrombocytopenic purpura

cachexia, dehydration, edema, hypercalcemia, hyperglycemia, hyperkalemia, hyperlipemia, hypocalcemia, hypoglycemia, ***Metabolic & Nutritional System:*** hypoglycemic reaction, hypokalemia, hypomagnesemia, hyponatremia, hypophosphatemia, hypoproteinemia, increased alkaline phosphatase, increased BUN, increased lactic dehydrogenase, increased SGOT, increased SGPT, peripheral edema, respiratory alkalosis, thirst, weight loss, weight gain

arthralgia, arthrosis, bone necrosis, bone pain, joint disorder, leg cramps, myalgia, myasthenia, pathological fracture ***Musculoskeletal System:***

abnormal dreams, abnormal gait, acute brain syndrome, agitation, amnesia, anxiety, ataxia, cerebrovascular disorder, confusion, convulsion, ***Nervous System:*** delirium, dementia, depression, dizziness, drug dependence, dry mouth, encephalopa-thy, facial paralysis, hallucinations, hemiplegia, hyperesthesia, hypertonia, hypotony, incoordination, increased libido, insomnia, myoclonus, nervousness, neuropathy, paresthesia, personality disorder, somnolence, speech disorder, tremor, twitching, vasodilatation, vertigo

asthma, bronchitis, epistaxis, hemoptysis, hiccup, hyperventilation, hypoxia, increased sputum, larynx edema, lung disorder, pharyngitis, ***Respiratory System:*** pneumothorax, rhinitis, sinusitis

acne, angioedema, dry skin, eczema, exfoliative dermatitis, furunculosis, herpes simplex, nail disorder, pruritus, rash, seborrhea, skin ***Skin & Appendages:*** discoloration, skin disorder, skin hypertrophy, skin ulcer, sweating, urticaria

abnormal vision, amblyopia, blindness, cataract, conjunctivitis, corneal lesion, corneal opacity, diplopia, dry eyes, ear disorder, ear pain, eye ***Special Senses:*** disorder, eye pain, hyperacusis, iritis, keratitis, miosis, otitis externa, otitis media, refraction disorder, retinal detachment, retinal disorder, taste perversion, tinnitus, uveitis, visual field defect, hearing loss

decreased creatinine clearance, dysuria, glycosuria, hematuria, kidney stone, mastitis, metorrhagia, nocturia, polyuria, prostatic disorder, toxic ***Urogenital System:*** nephrophathy, urethritis, urinary casts, urinary incontinence, urinary retention, urinary tract infection

Table 5. All Clinical Adverse Events, Laboratory Abnormalities or Intercurrent Illnesses Regardless of Severity Occurring in > 15% of Patients

# patients (%) [a] N =115	
115 (100)	Any Adverse Event
101 (88)	Proteinuria (? 30 mg/dL)
79 (69)	Nausea +/- Vomiting
67 (58)	Fever
50 (43)	Neutropenia (< 750 cells/mm^3)
50 (43)	Asthenia
34 (30)	Headache
34 (30)	Rash
32 (28)	Infection
31 (27)	Alopecia
30 (26)	Diarrhea
29 (25)	Pain
28 (24)	Creatinine Elevation (> 1.5 mg/dL)
28 (24)	Anemia
26 (23)	Anorexia
26 (23)	Dyspnea
25 (22)	Chills
22 (19)	Increased Cough
21 (18)	Oral Moniliasis

[a] Patients receiving 5 mg/kg maintenance regimen in Studies 106 and 107.

Reporting of Adverse Reactions

Malignancies or serious adverse reactions that occur in patients who have received VISTIDE (cidofovir) should be reported to Gilead in writing to the Director of Clinical Research, Gilead Sciences, Inc., 333 Lakeside Drive, Foster City, CA 94404 or by calling 1-800-GILEAD-5 (445-3235), or to FDA MedWatch 1-800-FDA-1088/fax 1-800-FDA-0178.