

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use VIDEX safely and effectively. See full prescribing information for VIDEX.

**VIDEX (didanosine, USP) Pediatric Powder for Oral Solution**  
Initial U.S. Approval: 1991

<p><b>WARNING: PANCREATITIS, LACTIC ACIDOSIS and HEPATOMEGALY with STEATOSIS</b></p> <p><i>See full prescribing information for complete boxed warning.</i></p> <ul style="list-style-type: none"> <li>• <b>Fatal and nonfatal pancreatitis. VIDEX should be suspended in patients with suspected pancreatitis and discontinued in patients with confirmed pancreatitis. (5.1)</b></li> <li>• <b>Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases. Fatal lactic acidosis has been reported in pregnant women who received the combination of didanosine and stavudine. (5.2)</b></li> </ul>
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-----**RECENT MAJOR CHANGES**-----

Dosage and Administration	
Dosage Adjustment (2.3)	06/2009
Contraindications	
Allopurinol (4.1)	06/2009
Ribavirin (4.2)	06/2009

-----**INDICATIONS AND USAGE**-----

VIDEX (didanosine, USP) is a nucleoside reverse transcriptase inhibitor for use in combination with other antiretroviral agents for the treatment of human immunodeficiency virus (HIV)-1 infection. (1)

-----**DOSAGE AND ADMINISTRATION**-----

- Adult patients: Administered on an empty stomach at least 30 minutes before or 2 hours after eating. Dosing is based on body weight. (2.1)

	<b>at least 60 kg</b>	<b>less than 60 kg</b>
Preferred dosing	200 mg twice daily	125 mg twice daily
Dosing for patients whose management requires once-daily frequency	400 mg once daily	250 mg once daily

- Pediatric patients (2 weeks old to 18 years old): Administered on an empty stomach at least 30 minutes before or 2 hours after eating.
  - Between 2 weeks and 8 months old, dosing is 100 mg/m<sup>2</sup> twice daily.
  - For those greater than 8 months old, dosing is 120 mg/m<sup>2</sup> twice daily but not to exceed the adult dosing recommendation. (2.1)
- Renal impairment: Dose reduction is recommended. (2.2)
- Coadministration with tenofovir: Dose reduction is recommended. Patients should be monitored closely for didanosine-associated adverse reactions. (2.3, 7.1)

-----**DOSAGE FORMS AND STRENGTHS**-----

- 4-ounce glass bottle containing 2 g of VIDEX (3)
- 8-ounce glass bottle containing 4 g of VIDEX (3)

-----**CONTRAINDICATIONS**-----

Coadministration with allopurinol or ribavirin is contraindicated. (4.1 and 4.2)

-----**WARNINGS AND PRECAUTIONS**-----

- Pancreatitis: Suspension or discontinuation of didanosine may be necessary. (5.1)
- Lactic acidosis and severe hepatomegaly with steatosis: Suspend didanosine in patients who develop clinical symptoms or signs with or without laboratory findings. (5.2)
- Hepatic toxicity: Interruption or discontinuation of didanosine must be considered upon worsening of liver disease. (5.3)
- Patients may develop peripheral neuropathy (5.4), retinal changes and optic neuritis (5.5), immune reconstitution syndrome (5.6), and redistribution/accumulation of body fat (5.7).

-----**ADVERSE REACTIONS**-----

- In adults, the most common adverse reactions (greater than 10%, all grades) are diarrhea, peripheral neurologic symptoms/neuropathy, abdominal pain, nausea, headache, rash, and vomiting. (6.1)
- Adverse reactions in pediatric patients were consistent with those in adults. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch)**

-----**DRUG INTERACTIONS**-----

Coadministration of VIDEX can alter the concentration of other drugs and other drugs may alter the concentration of didanosine. The potential drug-drug interactions must be considered prior to and during therapy. (4, 7, 12.3)

-----**USE IN SPECIFIC POPULATIONS**-----

Pregnancy: Fatal lactic acidosis has been reported in pregnant women who received both didanosine and stavudine with other agents. This combination should be used with caution during pregnancy and only if the potential benefit clearly outweighs the potential risk. (5.2, 8.1) Physicians are encouraged to register patients in the Antiretroviral Pregnancy Registry by calling 1-800-258-4263.

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**

**Revised: 06/2009**

**FULL PRESCRIBING INFORMATION: CONTENTS\***

**WARNING: PANCREATITIS, LACTIC ACIDOSIS AND**

**HEPATOMEGALY WITH STEATOSIS**

**1 INDICATIONS AND USAGE**

**2 DOSAGE AND ADMINISTRATION**

- 2.1 Recommended Dosage (Adult and Pediatric Patients)
- 2.2 Renal Impairment
- 2.3 Dosage Adjustment

**3 DOSAGE FORMS AND STRENGTHS**

**4 CONTRAINDICATIONS**

- 4.1 Allopurinol
- 4.2 Ribavirin

**5 WARNINGS AND PRECAUTIONS**

- 5.1 Pancreatitis
- 5.2 Lactic Acidosis/Severe Hepatomegaly with Steatosis
- 5.3 Hepatic Toxicity
- 5.4 Peripheral Neuropathy
- 5.5 Retinal Changes and Optic Neuritis
- 5.6 Immune Reconstitution Syndrome
- 5.7 Fat Redistribution

**6 ADVERSE REACTIONS**

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

**7 DRUG INTERACTIONS**

- 7.1 Established Drug Interactions
- 7.2 Predicted Drug Interactions

**8 USE IN SPECIFIC POPULATIONS**

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use

8.5 Geriatric Use

8.6 Renal Impairment

**10 OVERDOSAGE**

**11 DESCRIPTION**

**12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.3 Pharmacokinetics
- 12.4 Microbiology

**13 NONCLINICAL TOXICOLOGY**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

**14 CLINICAL STUDIES**

- 14.1 Adult Patients
- 14.2 Pediatric Patients

**16 HOW SUPPLIED/STORAGE AND HANDLING**

**17 PATIENT COUNSELING INFORMATION**

- 17.1 Pancreatitis
- 17.2 Peripheral Neuropathy
- 17.3 Lactic Acidosis and Severe Hepatomegaly with Steatosis
- 17.4 Hepatic Toxicity
- 17.5 Retinal Changes and Optic Neuritis
- 17.6 Fat Redistribution
- 17.7 Concomitant Therapy
- 17.8 General Information
- 17.9 FDA-Approved Patient Labeling

\*Sections or subsections omitted from the full prescribing information are not listed

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## 1 FULL PRESCRIBING INFORMATION

### **WARNING: PANCREATITIS, LACTIC ACIDOSIS and HEPATOMEGALY with STEATOSIS**

Fatal and nonfatal pancreatitis has occurred during therapy with VIDEX used alone or in combination regimens in both treatment-naive and treatment-experienced patients, regardless of degree of immunosuppression. VIDEX should be suspended in patients with suspected pancreatitis and discontinued in patients with confirmed pancreatitis [*see Warnings and Precautions (5.1)*].

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination, including didanosine and other antiretrovirals. Fatal lactic acidosis has been reported in pregnant women who received the combination of didanosine and stavudine with other antiretroviral agents. The combination of didanosine and stavudine should be used with caution during pregnancy and is recommended only if the potential benefit clearly outweighs the potential risk [*see Warnings and Precautions (5.2)*].

## 2 1 INDICATIONS AND USAGE

3 VIDEX<sup>®</sup> (didanosine, USP), also known as ddI, in combination with other antiretroviral  
4 agents is indicated for the treatment of human immunodeficiency virus (HIV)-1 infection  
5 [*see Clinical Studies (14)*].

## 6 2 DOSAGE AND ADMINISTRATION

7 VIDEX should be administered on an empty stomach, at least 30 minutes before or  
8 2 hours after eating.

### 9 2.1 Recommended Dosage (Adult and Pediatric Patients)

10 The preferred dosing frequency of VIDEX is twice daily because there is more evidence  
11 to support the effectiveness of this dosing regimen. Once-daily dosing should be  
12 considered only for patients whose management requires once-daily dosing of VIDEX

13 [see *Clinical Studies (14)*]. The recommended adult total daily dose is based on body  
14 weight (kg) (see Table 1).

**Table 1: Recommended Dosage (Adult)**

	at least 60 kg	less than 60 kg
Preferred dosing	200 mg twice daily	125 mg twice daily
Dosing for patients whose management requires once-daily frequency	400 mg once daily	250 mg once daily

15 **Pediatric Patients (2 weeks old to 18 years old):** The recommended dose of VIDEX  
16 (didanosine) in pediatric patients between 2 weeks old and 8 months old is 100 mg/m<sup>2</sup>  
17 twice daily, and the recommended VIDEX dose for pediatric patients greater than 8  
18 months old is 120 mg/m<sup>2</sup> twice daily but not to exceed the adult dosing recommendation.

19 Dosing recommendations in patients less than 2 weeks of age cannot be made because the  
20 pharmacokinetics of didanosine in these children are too variable to determine an  
21 appropriate dose. There are no data on once-daily dosing of VIDEX in pediatric patients.

## 22 2.2 Renal Impairment

### 23 Adult Patients

24 In adult patients with impaired renal function, the dose of VIDEX should be adjusted to  
25 compensate for the slower rate of elimination. The recommended doses and dosing  
26 intervals of VIDEX in adult patients with renal insufficiency are presented in Table 2.

**Table 2: Recommended Dosage in Patients with Renal Impairment**

Creatinine Clearance (mL/min)	Recommended VIDEX Dose by Patient Weight	
	at least 60 kg	less than 60 kg
at least 60	200 mg twice daily <sup>a</sup>	125 mg twice daily <sup>a</sup>
30-59	200 mg once daily or 100 mg twice daily	150 mg once daily or 75 mg twice daily
10-29	150 mg once daily	100 mg once daily
less than 10	100 mg once daily	75 mg once daily

<sup>a</sup> 400 mg once daily (at least 60 kg) or 250 mg once daily (less than 60 kg) for patients whose management requires once-daily frequency of administration.

27 **Pediatric Patients**

28 Urinary excretion is also a major route of elimination of didanosine in pediatric patients;  
29 therefore, the clearance of didanosine may be altered in pediatric patients with renal  
30 impairment. Although there are insufficient data to recommend a specific dose  
31 adjustment of VIDEX in this patient population, a reduction in the dose should be  
32 considered (see Table 2).

33 **Patients Requiring Continuous Ambulatory Peritoneal Dialysis (CAPD) or**  
34 **Hemodialysis**

35 For patients requiring CAPD or hemodialysis, follow dosing recommendations for  
36 patients with creatinine clearance of less than 10 mL/min, shown in Table 2. It is not  
37 necessary to administer a supplemental dose of VIDEX following hemodialysis.

38 **2.3 Dosage Adjustment**

39 **Concomitant Therapy with Tenofovir Disoproxil Fumarate**

40 In patients who are also taking tenofovir disoproxil fumarate, a dose reduction of VIDEX  
41 to 250 mg (adults weighing at least 60 kg with creatinine clearance of at least  
42 60 mL/min) or 200 mg (adults weighing less than 60 kg with creatinine clearance of at  
43 least 60 mL/min) once daily is recommended. VIDEX and tenofovir disoproxil fumarate  
44 may be taken together in the fasted state. Alternatively, if tenofovir disoproxil fumarate is  
45 taken with food, VIDEX should be taken on an empty stomach (at least 30 minutes  
46 before food or 2 hours after food). The appropriate dose of VIDEX coadministered with  
47 tenofovir disoproxil fumarate in patients with creatinine clearance of less than 60 mL/min  
48 has not been established. ([See *Drug Interactions* (7) and *Clinical Pharmacology* (12.3)];  
49 see the complete prescribing information for VIDEX EC (enteric-coated formulation of  
50 didanosine) for results of drug interaction studies of tenofovir disoproxil fumarate with  
51 reduced doses of the enteric-coated formulation of didanosine.)

52 **Hepatic Impairment**

53 No dose adjustment is required in patients with hepatic impairment [see *Warnings and*  
54 *Precautions* (5.3) and *Clinical Pharmacology* (12.3)].

55 **3 DOSAGE FORMS AND STRENGTHS**

56 VIDEX (didanosine, USP) Pediatric Powder for Oral Solution is supplied in 4- and  
57 8-ounce glass bottles containing 2 g or 4 g of VIDEX, respectively.

58 **4 CONTRAINDICATIONS**

59 These recommendations are based on either drug interaction studies or observed clinical  
60 toxicities.

61 **4.1 Allopurinol**

62 Coadministration of didanosine and allopurinol is contraindicated because systemic  
63 exposures of didanosine are increased, which may increase didanosine-associated toxicity  
64 [*see Clinical Pharmacology (12.3)*].

65 **4.2 Ribavirin**

66 Coadministration of didanosine and ribavirin is contraindicated because exposures of the  
67 active metabolite of didanosine (dideoxyadenosine 5'-triphosphate) are increased. Fatal  
68 hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic  
69 hyperlactatemia/lactic acidosis have been reported in patients receiving both didanosine  
70 and ribavirin.

71 **5 WARNINGS AND PRECAUTIONS**

72 **5.1 Pancreatitis**

73 **Fatal and nonfatal pancreatitis has occurred during therapy with VIDEX used**  
74 **alone or in combination regimens in both treatment-naive and treatment-**  
75 **experienced patients, regardless of degree of immunosuppression. VIDEX should be**  
76 **suspended in patients with signs or symptoms of pancreatitis and discontinued in**  
77 **patients with confirmed pancreatitis. Patients treated with VIDEX in combination**  
78 **with stavudine may be at increased risk for pancreatitis.**

79 When treatment with life-sustaining drugs known to cause pancreatic toxicity is required,  
80 suspension of VIDEX (didanosine) therapy is recommended. In patients with risk factors  
81 for pancreatitis, VIDEX should be used with extreme caution and only if clearly

82 indicated. Patients with advanced HIV-1 infection, especially the elderly, are at increased  
83 risk of pancreatitis and should be followed closely. Patients with renal impairment may  
84 be at greater risk for pancreatitis if treated without dose adjustment. The frequency of  
85 pancreatitis is dose related. [*See Adverse Reactions (6).*]

## 86 **5.2 Lactic Acidosis/Severe Hepatomegaly with Steatosis**

87 **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have**  
88 **been reported with the use of nucleoside analogues alone or in combination,**  
89 **including didanosine and other antiretrovirals.** A majority of these cases have been in  
90 women. Obesity and prolonged nucleoside exposure may be risk factors. Fatal lactic  
91 acidosis has been reported in pregnant women who received the combination of  
92 didanosine and stavudine with other antiretroviral agents. The combination of didanosine  
93 and stavudine should be used with caution during pregnancy and is recommended only if  
94 the potential benefit clearly outweighs the potential risk [*see Use in Specific Populations*  
95 *(8.1)*]. Particular caution should be exercised when administering VIDEX to any patient  
96 with known risk factors for liver disease; however, cases have also been reported in  
97 patients with no known risk factors. Treatment with VIDEX should be suspended in any  
98 patient who develops clinical signs or symptoms with or without laboratory findings  
99 consistent with symptomatic hyperlactatemia, lactic acidosis, or pronounced  
100 hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of  
101 marked transaminase elevations).

## 102 **5.3 Hepatic Toxicity**

103 The safety and efficacy of VIDEX have not been established in HIV-infected patients  
104 with significant underlying liver disease. During combination antiretroviral therapy,  
105 patients with preexisting liver dysfunction, including chronic active hepatitis, have an  
106 increased frequency of liver function abnormalities, including severe and potentially fatal  
107 hepatic adverse events, and should be monitored according to standard practice. If there  
108 is evidence of worsening liver disease in such patients, interruption or discontinuation of  
109 treatment must be considered.

110 Hepatotoxicity and hepatic failure resulting in death were reported during postmarketing  
111 surveillance in HIV-infected patients treated with hydroxyurea and other antiretroviral  
112 agents. Fatal hepatic events were reported most often in patients treated with the

113 combination of hydroxyurea, didanosine, and stavudine. This combination should be  
114 avoided. [*See Adverse Reactions (6).*]

#### 115 **5.4 Peripheral Neuropathy**

116 Peripheral neuropathy, manifested by numbness, tingling, or pain in the hands or feet, has  
117 been reported in patients receiving VIDEX therapy. Peripheral neuropathy has occurred  
118 more frequently in patients with advanced HIV disease, in patients with a history of  
119 neuropathy, or in patients being treated with neurotoxic drug therapy, including  
120 stavudine. Discontinuation of VIDEX should be considered in patients who develop  
121 peripheral neuropathy. [*See Adverse Reactions (6).*]

#### 122 **5.5 Retinal Changes and Optic Neuritis**

123 Retinal changes and optic neuritis have been reported in adult and pediatric patients.  
124 Periodic retinal examinations should be considered for patients receiving VIDEX [*see*  
125 *Adverse Reactions (6)*].

#### 126 **5.6 Immune Reconstitution Syndrome**

127 Immune reconstitution syndrome has been reported in patients treated with combination  
128 antiretroviral therapy, including VIDEX. During the initial phase of combination  
129 antiretroviral treatment, patients whose immune system responds may develop an  
130 inflammatory response to indolent or residual opportunistic infections (such as  
131 *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jiroveci* pneumonia  
132 [PCP], or tuberculosis), which may necessitate further evaluation and treatment.

#### 133 **5.7 Fat Redistribution**

134 Redistribution/accumulation of body fat including central obesity, dorsocervical fat  
135 enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and  
136 “cushingoid appearance” have been observed in patients receiving antiretroviral therapy.  
137 The mechanism and long-term consequences of these events are currently unknown. A  
138 causal relationship has not been established.

139 **6 ADVERSE REACTIONS**

140 The following adverse reactions are discussed in greater detail in other sections:

- 141 • Pancreatitis [see *Boxed Warning, Warnings and Precautions (5.1)*]
- 142 • Lactic acidosis/severe hepatomegaly with steatosis [see *Boxed Warning, Warnings*  
143 *and Precautions (5.2)*]
- 144 • Hepatic toxicity [see *Warnings and Precautions (5.3)*]
- 145 • Peripheral neuropathy [see *Warnings and Precautions (5.4)*]
- 146 • Retinal changes and optic neuritis [see *Warnings and Precautions (5.5)*]

147 **6.1 Clinical Trials Experience**

148 Because clinical trials are conducted under widely varying conditions, adverse reaction  
149 rates observed in the clinical trials of a drug cannot be directly compared to rates in the  
150 clinical trials of another drug and may not reflect the rates observed in practice.

151 **Adults**

152 Selected clinical adverse reactions that occurred in adult patients in clinical studies with  
153 VIDEX are provided in Tables 3 and 4.

**Table 3: Selected Clinical Adverse Reactions from Monotherapy Studies**

Adverse Reactions	Percent of Patients*			
	ACTG 116A		ACTG 116B/117	
	VIDEX n=197	zidovudine n=212	VIDEX n=298	zidovudine n=304
Diarrhea	19	15	28	21
Peripheral Neurologic Symptoms/Neuropathy	17	14	20	12
Abdominal Pain	13	8	7	8
Rash/Pruritus	7	8	9	5
Pancreatitis	7	3	6	2

\* The incidences reported included all severity grades and all reactions regardless of causality.

154

**Table 4: Selected Clinical Adverse Reactions from Combination Studies**

Adverse Reactions	Percent of Patients <sup>a,c</sup>			
	AI454-148 <sup>b</sup>		START 2 <sup>b</sup>	
	VIDEX + stavudine + nelfinavir n=482	zidovudine + lamivudine + nelfinavir n=248	VIDEX + stavudine + indinavir n=102	zidovudine + lamivudine + indinavir n=103
Diarrhea	70	60	45	39
Nausea	28	40	53	67
Peripheral Neurologic Symptoms/Neuropathy	26	6	21	10
Headache	21	30	46	37
Rash	13	16	30	18
Vomiting	12	14	30	35
Pancreatitis (see below)	1	*	less than 1	*

<sup>a</sup> Percentages based on treated subjects.

<sup>b</sup> Median duration of treatment 48 weeks.

<sup>c</sup> The incidences reported included all severity grades and all reactions regardless of causality.

\* This event was not observed in this study arm.

155 Pancreatitis resulting in death was observed in one patient who received VIDEX  
 156 (didanosine) plus stavudine plus nelfinavir in Study AI454-148 and in one patient who  
 157 received VIDEX plus stavudine plus indinavir in the START 2 study. In addition,  
 158 pancreatitis resulting in death was observed in 2 of 68 patients who received VIDEX plus  
 159 stavudine plus indinavir plus hydroxyurea in an ACTG clinical trial [*see Warnings and*  
 160 *Precautions (5)*].

161 The frequency of pancreatitis is dose related. In phase 3 studies, incidence ranged from  
 162 1% to 10% with doses higher than are currently recommended and from 1% to 7% with  
 163 recommended dose.

164 Selected laboratory abnormalities in clinical studies with VIDEX are shown in  
 165 Tables 5-7.

**Table 5: Selected Laboratory Abnormalities from Monotherapy Studies**

Parameter	Percent of Patients			
	ACTG 116A		ACTG 116B/117	
	VIDEX n=197	zidovudine n=212	VIDEX n=298	zidovudine n=304
SGOT (AST) (greater than 5 x ULN)	9	4	7	6
SGPT (ALT) (greater than 5 x ULN)	9	6	6	6
Alkaline phosphatase (greater than 5 x ULN)	4	1	1	1
Amylase (at least 1.4 x ULN)	17	12	15	5
Uric acid (greater than 12 mg/dL)	3	1	2	1

ULN = upper limit of normal.

166

**Table 6: Selected Laboratory Abnormalities from Combination Studies (Grades 3-4)**

Parameter	Percent of Patients <sup>a</sup>			
	AI454-148 <sup>b</sup>		START 2 <sup>b</sup>	
	VIDEX + stavudine + nelfinavir n=482	zidovudine + lamivudine + nelfinavir n=248	VIDEX + stavudine + indinavir n=102	zidovudine + lamivudine + indinavir n=103
Bilirubin (greater than 2.6 x ULN)	less than 1	less than 1	16	8
SGOT (AST) (greater than 5 x ULN)	3	2	7	7
SGPT (ALT) (greater than 5 x ULN)	3	3	8	5
GGT (greater than 5 x ULN)	NC	NC	5	2
Lipase (greater than 2 x ULN)	7	2	5	5
Amylase (greater than 2 x ULN)	NC	NC	8	2

ULN = upper limit of normal.

NC = Not Collected.

<sup>a</sup> Percentages based on treated subjects.

<sup>b</sup> Median duration of treatment 48 weeks.

167

**Table 7: Selected Laboratory Abnormalities from Combination Studies (All Grades)**

Parameter	Percent of Patients <sup>a</sup>			
	AI454-148 <sup>b</sup>		START 2 <sup>b</sup>	
	VIDEX + stavudine + nelfinavir n=482	zidovudine + lamivudine + nelfinavir n=248	VIDEX + stavudine + indinavir n=102	zidovudine + lamivudine + indinavir n=103
Bilirubin	7	3	68	55
SGOT (AST)	42	23	53	20
SGPT (ALT)	37	24	50	18
GGT	NC	NC	28	12
Lipase	17	11	26	19
Amylase	NC	NC	31	17

NC = Not Collected.

<sup>a</sup> Percentages based on treated subjects.

<sup>b</sup> Median duration of treatment 48 weeks.

## 168 **Pediatric Patients**

169 In clinical trials, 743 pediatric patients between 2 weeks and 18 years of age have been  
170 treated with didanosine. Adverse reactions and laboratory abnormalities reported to occur  
171 in these patients were generally consistent with the safety profile of didanosine in adults.

172 In pediatric phase 1 studies, pancreatitis occurred in 2 of 60 (3%) patients treated at entry  
173 doses below 300 mg/m<sup>2</sup>/day and in 5 of 38 (13%) patients treated at higher doses. In  
174 study ACTG 152, pancreatitis occurred in none of the 281 pediatric patients who received  
175 didanosine 120 mg/m<sup>2</sup> every 12 hours and in less than 1% of the 274 pediatric patients  
176 who received didanosine 90 mg/m<sup>2</sup> every 12 hours in combination with zidovudine [*see*  
177 *Clinical Studies (14)*].

178 Retinal changes and optic neuritis have been reported in pediatric patients.

## 179 **6.2 Postmarketing Experience**

180 The following adverse reactions have been identified during postapproval use of  
181 didanosine. Because they are reported voluntarily from a population of unknown size,  
182 estimates of frequency cannot be made. These reactions have been chosen for inclusion  
183 due to their seriousness, frequency of reporting, causal connection to VIDEX, or a  
184 combination of these factors.

185 *Blood and Lymphatic System Disorders* – anemia, leukopenia, and  
186 thrombocytopenia.

187 *Body as a Whole* – alopecia, anaphylactoid reaction, asthenia, chills/fever, pain,  
188 and redistribution/accumulation of body fat [*see Warnings and Precautions (5.7)*].

189 *Digestive Disorders* – anorexia, dyspepsia, and flatulence.

190 *Exocrine Gland Disorders* – pancreatitis (including fatal cases) [*see Boxed*  
191 *Warning, Warnings and Precautions (5.1)*], sialoadenitis, parotid gland  
192 enlargement, dry mouth, and dry eyes.

193 *Hepatobiliary Disorders* – symptomatic hyperlactatemia/lactic acidosis and  
194 hepatic steatosis [*see Boxed Warning, Warnings and Precautions (5.2)*]; hepatitis  
195 and liver failure.

196 *Metabolic Disorders* – diabetes mellitus, hypoglycemia, and hyperglycemia.

197 *Musculoskeletal Disorders* – myalgia (with or without increases in creatine  
198 kinase), rhabdomyolysis including acute renal failure and hemodialysis,  
199 arthralgia, and myopathy.

200 *Ophthalmologic Disorders* – retinal depigmentation and optic neuritis [*see*  
201 *Warnings and Precautions (5.5)*].

### 202 **Use with Stavudine- and Hydroxyurea-Based Regimens**

203 When didanosine is used in combination with other agents with similar toxicities, the  
204 incidence of these toxicities may be higher than when didanosine is used alone. Thus,  
205 patients treated with VIDEX in combination with stavudine, with or without  
206 hydroxyurea, may be at increased risk for pancreatitis and hepatotoxicity, which may be

207 fatal, and severe peripheral neuropathy [*see Warnings and Precautions (5)*]. The  
208 combination of VIDEX and hydroxyurea, with or without stavudine, should be avoided.

## 209 **7 DRUG INTERACTIONS**

### 210 **7.1 Established Drug Interactions**

211 Clinical recommendations based on the results of drug interaction studies are listed in  
212 Table 8. Pharmacokinetic results of drug interactions studies are shown in Tables 12 and  
213 13 [*see Contraindications (4.1 and 4.2), Clinical Pharmacology (12.3)*].

**Table 8: Established Drug Interactions with VIDEX**

<b>Drug</b>	<b>Effect</b>	<b>Clinical Comment</b>
ciprofloxacin	↓ ciprofloxacin concentration	Administer VIDEX at least 2 hours after or 6 hours before ciprofloxacin.
delavirdine	↓ delavirdine concentration	Administer VIDEX 1 hour after delavirdine.
ganciclovir	↑ didanosine concentration	If there is no suitable alternative to ganciclovir, then use in combination with VIDEX with caution. Monitor for didanosine-associated toxicity.
indinavir	↓ indinavir concentration	Administer VIDEX 1 hour after indinavir.
methadone	↓ didanosine concentration	Do not coadminister methadone with VIDEX pediatric powder due to significant decreases in didanosine concentrations. If coadministration of methadone and didanosine is necessary, the recommended formulation of didanosine is VIDEX EC. Patients should be closely monitored for adequate clinical response when VIDEX EC is coadministered with methadone, including monitoring for changes in HIV RNA viral load.
nelfinavir	No interaction 1 hour after didanosine	Administer nelfinavir 1 hour after VIDEX.

**Table 8: Established Drug Interactions with VIDEX**

Drug	Effect	Clinical Comment
tenofovir disoproxil fumarate	↑ didanosine concentration	<p>A dose reduction of VIDEX to the following dosage once daily is recommended.<sup>a</sup></p> <ul style="list-style-type: none"><li>• 250 mg (adults weighing at least 60 kg with creatinine clearance of at least 60 mL/min)</li><li>• 200 mg (adults weighing less than 60 kg with creatinine clearance of at least 60 mL/min)</li></ul> <p>VIDEX and tenofovir disoproxil fumarate may be taken together in the fasted state. If tenofovir disoproxil fumarate is taken with food, VIDEX should be taken on an empty stomach (at least 30 minutes before food or 2 hours after food). Patients should be monitored for didanosine-associated toxicities and clinical response.</p>

↑ Indicates increase.

↓ Indicates decrease.

<sup>a</sup> The dosing recommendation for coadministration of VIDEX EC and tenofovir disoproxil fumarate with respect to meal consumption differs from that of VIDEX. See the complete prescribing information for VIDEX EC.

214 Exposure to didanosine is increased when coadministered with tenofovir disoproxil  
215 fumarate [Table 8 and *see Clinical Pharmacokinetics (12.3, Table 12)*]. Increased  
216 exposure may cause or worsen didanosine-related clinical toxicities, including  
217 pancreatitis, symptomatic hyperlactatemia/lactic acidosis, and peripheral neuropathy.  
218 Coadministration of tenofovir disoproxil fumarate with VIDEX should be undertaken  
219 with caution, and patients should be monitored closely for didanosine-related toxicities  
220 and clinical response. VIDEX should be suspended if signs or symptoms of pancreatitis,  
221 symptomatic hyperlactatemia, or lactic acidosis develop [*see Dosage and Administration*  
222 *(2.3), Warnings and Precautions (5)*]. Suppression of CD4 cell counts has been observed  
223 in patients receiving tenofovir disoproxil fumarate with didanosine at a dose of 400 mg  
224 daily.

## 225 **7.2 Predicted Drug Interactions**

226 Predicted drug interactions with VIDEX are listed in Table 9.

**Table 9: Predicted Drug Interactions with VIDEX**

Drug or Drug Class	Effect	Clinical Comment
Drugs that may cause pancreatic toxicity	↑ risk of pancreatitis	Use only with extreme caution <sup>a</sup>
Neurotoxic drugs	↑ risk of neuropathy	Use with caution <sup>b</sup>
Antacids containing magnesium or aluminum	↑ side effects associated with antacid components	Use caution with VIDEX Pediatric Powder for Oral Solution
Azole antifungals	↓ ketoconazole or itraconazole concentration	Administer drugs such as ketoconazole or itraconazole at least 2 hours before VIDEX.
Quinolone antibiotics (see also ciprofloxacin in Table 8)	↓ quinolone concentration	Consult package insert of the quinolone.
Tetracycline antibiotics	↓ antibiotic concentration	Consult package insert of the tetracycline.

↑ Indicates increase.

↓ Indicates decrease.

<sup>a</sup> Only if other drugs are not available and if clearly indicated. If treatment with life-sustaining drugs that cause pancreatic toxicity is required, suspension of VIDEX is recommended [*see Warnings and Precautions (5.1)*].

<sup>b</sup> [*See Warnings and Precautions (5.5)*].

## 227 **8 USE IN SPECIFIC POPULATIONS**

### 228 **8.1 Pregnancy**

#### 229 **Pregnancy Category B**

230 Reproduction studies have been performed in rats and rabbits at doses up to 12 and  
 231 14.2 times the estimated human exposure (based upon plasma levels), respectively, and  
 232 have revealed no evidence of impaired fertility or harm to the fetus due to didanosine. At  
 233 approximately 12 times the estimated human exposure, didanosine was slightly toxic to  
 234 female rats and their pups during mid and late lactation. These rats showed reduced food  
 235 intake and body weight gains but the physical and functional development of the  
 236 offspring was not impaired and there were no major changes in the F2 generation. A  
 237 study in rats showed that didanosine and/or its metabolites are transferred to the fetus  
 238 through the placenta. Animal reproduction studies are not always predictive of human  
 239 response.

240 There are no adequate and well-controlled studies of didanosine in pregnant women.  
241 Didanosine should be used during pregnancy only if the potential benefit justifies the  
242 potential risk.

243 Fatal lactic acidosis has been reported in pregnant women who received the combination  
244 of didanosine and stavudine with other antiretroviral agents. It is unclear if pregnancy  
245 augments the risk of lactic acidosis/hepatic steatosis syndrome reported in nonpregnant  
246 individuals receiving nucleoside analogues [*see Warnings and Precautions (5.2)*]. **The**  
247 **combination of didanosine and stavudine should be used with caution during**  
248 **pregnancy and is recommended only if the potential benefit clearly outweighs the**  
249 **potential risk.** Healthcare providers caring for HIV-infected pregnant women receiving  
250 didanosine should be alert for early diagnosis of lactic acidosis/hepatic steatosis  
251 syndrome.

### 252 **Antiretroviral Pregnancy Registry**

253 To monitor maternal-fetal outcomes of pregnant women exposed to didanosine and other  
254 antiretroviral agents, an Antiretroviral Pregnancy Registry has been established.  
255 Physicians are encouraged to register patients by calling 1-800-258-4263.

## 256 **8.3 Nursing Mothers**

257 **The Centers for Disease Control and Prevention recommend that HIV-infected**  
258 **mothers not breast-feed their infants to avoid risking postnatal transmission of HIV.**  
259 A study in rats showed that following oral administration, didanosine and/or its  
260 metabolites were excreted into the milk of lactating rats. It is not known if didanosine is  
261 excreted in human milk. Because of both the potential for HIV transmission and the  
262 potential for serious adverse reactions in nursing infants, **mothers should be instructed**  
263 **not to breast-feed if they are receiving didanosine.**

## 264 **8.4 Pediatric Use**

265 Use of didanosine in pediatric patients from 2 weeks of age through adolescence is  
266 supported by evidence from adequate and well-controlled studies of VIDEX in adult and  
267 pediatric patients [*see Dosage and Administration (2), Adverse Reactions (6.1), Clinical*  
268 *Pharmacology (12.3), and Clinical Studies (14)*].

## 269 **8.5 Geriatric Use**

270 In an Expanded Access Program for patients with advanced HIV infection, patients aged  
271 65 years and older had a higher frequency of pancreatitis (10%) than younger patients  
272 (5%) [*see Warnings and Precautions (5.1)*]. Clinical studies of didanosine did not include  
273 sufficient numbers of subjects aged 65 years and over to determine whether they respond  
274 differently than younger subjects. Didanosine is known to be substantially excreted by  
275 the kidney, and the risk of toxic reactions to this drug may be greater in patients with  
276 impaired renal function. Because elderly patients are more likely to have decreased renal  
277 function, care should be taken in dose selection. In addition, renal function should be  
278 monitored and dosage adjustments should be made accordingly [*see Dosage and*  
279 *Administration (2.2)*].

## 280 **8.6 Renal Impairment**

281 Patients with renal impairment (creatinine clearance of less than 60 mL/min) may be at  
282 greater risk of toxicity from didanosine due to decreased drug clearance [*see Clinical*  
283 *Pharmacology (12.3)*]. A dose reduction is recommended for these patients [*see Dosage*  
284 *and Administration (2)*].

## 285 **10 OVERDOSAGE**

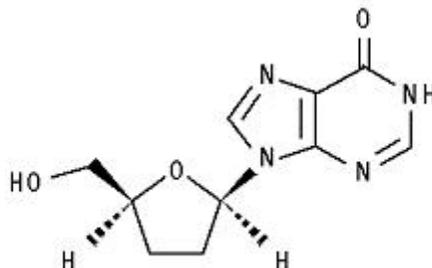
286 There is no known antidote for VIDEX (didanosine) overdosage. In phase 1 studies, in  
287 which VIDEX was initially administered at doses ten times the currently recommended  
288 dose, toxicities included: pancreatitis, peripheral neuropathy, diarrhea, hyperuricemia,  
289 and hepatic dysfunction. Didanosine is not dialyzable by peritoneal dialysis, although  
290 there is some clearance by hemodialysis [*see Clinical Pharmacology (12.3)*].

## 291 **11 DESCRIPTION**

292 VIDEX<sup>®</sup> is a brand name for didanosine, USP, a synthetic purine nucleoside analogue  
293 active against HIV-1.

294 Didanosine is available as VIDEX, a Pediatric Powder for Oral Solution [*see How*  
295 *Supplied/Storage and Handling (16)*] and as VIDEX<sup>®</sup> EC Delayed-Release Capsules,  
296 containing enteric-coated beadlets [consult prescribing information for VIDEX EC  
297 (didanosine)].

298 The chemical name for didanosine is 2',3'-dideoxyinosine. The structural formula is:



299 Didanosine is a white crystalline powder with the molecular formula  $C_{10}H_{12}N_4O_3$  and a  
300 molecular weight of 236.2. The aqueous solubility of didanosine at  $25^\circ C$  and pH of  
301 approximately 6 is 27.3 mg/mL. Didanosine is unstable in acidic solutions. For example,  
302 at pH less than 3 and  $37^\circ C$ , 10% of didanosine decomposes to hypoxanthine in less than  
303 2 minutes.

## 304 **12 CLINICAL PHARMACOLOGY**

### 305 **12.1 Mechanism of Action**

306 Didanosine is an antiviral agent [*see Clinical Pharmacology (12.4)*].

### 307 **12.3 Pharmacokinetics**

308 The pharmacokinetic parameters of didanosine are summarized in Table 10. Didanosine  
309 is rapidly absorbed, with peak plasma concentrations generally observed from 0.25 to  
310 1.50 hours following oral dosing. Increases in plasma didanosine concentrations were  
311 dose proportional over the range of 50 to 400 mg. Steady-state pharmacokinetic  
312 parameters did not differ significantly from values obtained after a single dose. Binding  
313 of didanosine to plasma proteins *in vitro* was low (less than 5%). Based on data from  
314 *in vitro* and animal studies, it is presumed that the metabolism of didanosine in man  
315 occurs by the same pathways responsible for the elimination of endogenous purines.

**Table 10: Mean ± SD Pharmacokinetic Parameters for Didanosine in Adult and Pediatric Patients**

Parameter	Adult Patients <sup>a</sup>	n	Pediatric Patients <sup>b</sup>			
			8 months to 19 years	n	2 weeks to 4 months	n
Oral bioavailability (%)	42 ± 12	6	25 ± 20	46	ND	
Apparent volume of distribution <sup>c</sup> (L/m <sup>2</sup> )	43.70 ± 8.90	6	28 ± 15	49	ND	
CSF-plasma ratio <sup>d</sup>	21 ± 0.03% <sup>e</sup>	5	46% (range 12-85%)	7	ND	
Systemic clearance <sup>c</sup> (mL/min/m <sup>2</sup> )	526 ± 64.7	6	516 ± 184	49	ND	
Renal clearance <sup>f</sup> (mL/min/m <sup>2</sup> )	223 ± 85.0	6	240 ± 90	15	ND	
Apparent oral clearance <sup>g</sup> (mL/min/m <sup>2</sup> )	1252 ± 154	6	2064 ± 736	48	1353 ± 759	41
Elimination half-life <sup>f</sup> (h)	1.5 ± 0.4	6	0.8 ± 0.3	60	1.2 ± 0.3	21
Urinary recovery of didanosine <sup>f</sup> (%)	18 ± 8	6	18 ± 10	15	ND	

CSF = cerebrospinal fluid, ND = not determined.

<sup>a</sup> Parameter units for adults were converted to the same units in pediatric patients to facilitate comparisons among populations: mean adult body weight = 70 kg and mean adult body surface area = 1.73 m<sup>2</sup>.

<sup>b</sup> In 1-day old infants (n=10), the mean ± SD apparent oral clearance was 1523 ± 1176 mL/min/m<sup>2</sup> and half-life was 2.0 ± 0.7 h.

<sup>c</sup> Following IV administration.

<sup>d</sup> Following IV administration in adults and IV or oral administration in pediatric patients.

<sup>e</sup> Mean ± SE.

<sup>f</sup> Following oral administration.

<sup>g</sup> Apparent oral clearance estimate was determined as the ratio of the mean systemic clearance and the mean oral bioavailability estimate.

### 316 Effect of Food

317 Didanosine peak plasma concentrations (C<sub>max</sub>) and area under the plasma concentration  
 318 time curve (AUC) were decreased by approximately 55% when VIDEX tablets were  
 319 administered up to 2 hours after a meal. Administration of VIDEX tablets up to

320 30 minutes before a meal did not result in any significant changes in bioavailability [see  
321 *Dosage and Administration (2)*]. VIDEX should be taken on an empty stomach.

### 322 **Special Populations**

323 *Renal Insufficiency:* Data from two studies in adults indicated that the apparent oral  
324 clearance of didanosine decreased and the terminal elimination half-life increased as  
325 creatinine clearance decreased (see Table 11). Following oral administration, didanosine  
326 was not detectable in peritoneal dialysate fluid (n=6); recovery in hemodialysate (n=5)  
327 ranged from 0.6% to 7.4% of the dose over a 3-4 hour dialysis period. The absolute  
328 bioavailability of didanosine was not affected in patients requiring dialysis. [See *Dosage*  
329 *and Administration (2.2)*.]

**Table 11: Mean ± SD Pharmacokinetic Parameters for Didanosine Following a Single Oral Dose**

Parameter	Creatinine Clearance (mL/min)				Dialysis Patients n=11
	at least 90 n=12	60-90 n=6	30-59 n=6	10-29 n=3	
CL <sub>cr</sub> (mL/min)	112 ± 22	68 ± 8	46 ± 8	13 ± 5	ND
CL/F (mL/min)	2164 ± 638	1566 ± 833	1023 ± 378	628 ± 104	543 ± 174
CL <sub>R</sub> (mL/min)	458 ± 164	247 ± 153	100 ± 44	20 ± 8	less than 10
T <sub>1/2</sub> (h)	1.42 ± 0.33	1.59 ± 0.13	1.75 ± 0.43	2.0 ± 0.3	4.1 ± 1.2

ND = not determined due to anuria.

CL<sub>cr</sub> = creatinine clearance.

CL/F = apparent oral clearance.

CL<sub>R</sub> = renal clearance.

330 *Hepatic Impairment:* The pharmacokinetics of didanosine have been studied in 12 non-  
331 HIV-infected subjects with moderate (n=8) to severe (n=4) hepatic impairment (Child-  
332 Pugh Class B or C). Mean AUC and C<sub>max</sub> values following a single 400 mg dose of  
333 didanosine were approximately 13% and 19% higher, respectively, in patients with  
334 hepatic impairment compared to matched healthy subjects. No dose adjustment is needed,  
335 because a similar range and distribution of AUC and C<sub>max</sub> values was observed for  
336 subjects with hepatic impairment and matched healthy controls. [See *Dosage and*  
337 *Administration (2.3)*.]

338 *Pediatric Patients:* The pharmacokinetics of didanosine have been evaluated in HIV-  
 339 exposed and HIV-infected pediatric patients from birth to adulthood. Overall, the  
 340 pharmacokinetics of didanosine in pediatric patients are similar to those of didanosine in  
 341 adults. Didanosine plasma concentrations appear to increase in proportion to oral doses  
 342 ranging from 25 to 120 mg/m<sup>2</sup> in pediatric patients less than 5 months old and from 80 to  
 343 180 mg/m<sup>2</sup> in children above 8 months old. For information on controlled clinical studies  
 344 in pediatric patients, *see Clinical Studies (14.2) and Use in Specific Populations (8.4).*

345 *Geriatric Patients:* Didanosine pharmacokinetics have not been studied in patients over  
 346 65 years of age [*see Use in Specific Populations (8.5)*].

347 *Gender:* The effects of gender on didanosine pharmacokinetics have not been studied.

### 348 **Drug Interactions**

349 Tables 12 and 13 summarize the effects on AUC and C<sub>max</sub>, with a 95% confidence  
 350 interval (CI) when available, following coadministration of VIDEX (didanosine) with a  
 351 variety of drugs. Drug-drug interactions for VIDEX buffered tablets are applicable to the  
 352 VIDEX pediatric powder formulation and are noted in Tables 12 and 13. For clinical  
 353 recommendations based on drug interaction studies for drugs in bold font, see *Dosage*  
 354 *and Administration (2.3 for Concomitant Therapy with Tenofovir Disoproxil Fumarate)*  
 355 *and Drug Interactions (7.3).*

**Table 12: Results of Drug Interaction Studies with VIDEX: Effects of Coadministered Drug on Didanosine Plasma AUC and C<sub>max</sub> Values**

Drug	Didanosine Dosage	n	% Change of Didanosine Pharmacokinetic Parameters <sup>a</sup>	
			AUC of Didanosine (95% CI)	C <sub>max</sub> of Didanosine (95% CI)
allopurinol, renally impaired, 300 mg/day	200 mg single dose	2	↑ 312%	↑ 232%
healthy volunteer, 300 mg/day for 7 days	400 mg single dose	14	↑ 113%	↑ 69%
ciprofloxacin, 750 mg every 12 hours for 3 days, 2 hours before didanosine	200 mg every 12 hours for 3 days	8 <sup>b</sup>	↓ 16%	↓ 28%

**Table 12: Results of Drug Interaction Studies with VIDEX: Effects of Coadministered Drug on Didanosine Plasma AUC and C<sub>max</sub> Values**

Drug	Didanosine Dosage	n	% Change of Didanosine Pharmacokinetic Parameters <sup>a</sup>	
			AUC of Didanosine (95% CI)	C <sub>max</sub> of Didanosine (95% CI)
ganciclovir, 1000 mg every 8 hours, 2 hours after didanosine	200 mg every 12 hours	12	↑ 111%	NA
indinavir, 800 mg single dose, simultaneous	200 mg single dose	16	↔	↔
1 hour before didanosine	200 mg single dose	16	↓ 17% (-27, -7%) <sup>c</sup>	↓ 13% (-28, 5%) <sup>c</sup>
ketoconazole, 200 mg/day for 4 days, 2 hours before didanosine	375 mg every 12 hours for 4 days	12 <sup>b</sup>	↔	↓ 12%
methadone, chronic maintenance dose <sup>f</sup>	200 mg single dose	16 <sup>d</sup>	↓ 57%	↓ 66%
	400 mg single dose	15,16 <sup>e</sup>	↓ 29% (-40, -16%) <sup>c</sup>	↓ 41% (-54, -26%) <sup>c</sup>
tenofovir, <sup>g,h</sup> 300 mg once daily, 1 hour after didanosine	250 <sup>i</sup> or 400 mg once daily for 7 days	14	↑ 44% (31, 59%) <sup>c</sup>	↑ 28% (11, 48%) <sup>c</sup>
loperamide, 4 mg every 6 hours for 1 day	300 mg single dose	12 <sup>b</sup>	↔	↓ 23%
metoclopramide, 10 mg single dose	300 mg single dose	12 <sup>b</sup>	↔	↑ 13%
ranitidine, 150 mg single dose, 2 hours before didanosine	375 mg single dose	12 <sup>b</sup>	↑ 14%	↑ 13%
rifabutin, 300 or 600 mg/day for 12 days	167 or 250 mg every 12 hours for 12 days	11	↑ 13% (-1, 27%)	↑ 17% (-4, 38%)
ritonavir, 600 mg every 12 hours for 4 days	200 mg every 12 hours for 4 days	12	↓ 13% (0, 23%)	↓ 16% (5, 26%)
stavudine, 40 mg every 12 hours for 4 days	100 mg every 12 hours for 4 days	10	↔	↔
sulfamethoxazole, 1000 mg single dose	200 mg single dose	8 <sup>b</sup>	↔	↔
trimethoprim, 200 mg single dose	200 mg single dose	8 <sup>b</sup>	↔	↑ 17% (-23, 77%)
zidovudine, 200 mg every 8 hours for 3 days	200 mg every 12 hours for 3 days	6 <sup>b</sup>	↔	↔

↑ Indicates increase.

↓ Indicates decrease.

↔ Indicates no change, or mean increase or decrease of less than 10%.

**Table 12: Results of Drug Interaction Studies with VIDEX: Effects of Coadministered Drug on Didanosine Plasma AUC and C<sub>max</sub> Values**

Drug	Didanosine Dosage	n	% Change of Didanosine Pharmacokinetic Parameters <sup>a</sup>	
			AUC of Didanosine (95% CI)	C <sub>max</sub> of Didanosine (95% CI)

<sup>a</sup> The 95% confidence intervals for the percent change in the pharmacokinetic parameter are displayed.

<sup>b</sup> HIV-infected patients.

<sup>c</sup> 90% CI.

<sup>d</sup> Comparisons are made to a parallel control group not receiving methadone (n=10).

<sup>e</sup> Comparisons are made to historical controls (n=68, pooled from 3 studies) conducted in healthy subjects. The number of subjects evaluated for AUC and C<sub>max</sub> is 15 and 16, respectively.

<sup>f</sup> For results of drug interaction studies between the enteric-coated formulation of didanosine (VIDEX EC) and methadone, see the complete prescribing information for VIDEX EC.

<sup>g</sup> Tenofovir disoproxil fumarate.

<sup>h</sup> For results of drug interaction studies between the enteric-coated formulation of didanosine (VIDEX EC) and tenofovir disoproxil fumarate, see the complete prescribing information for VIDEX EC.

<sup>i</sup> Patients less than 60 kg with creatinine clearance of at least 60 mL/min.

NA = Not available.

356

**Table 13: Results of Drug Interaction Studies with VIDEX: Effects of Didanosine on Coadministered Drug Plasma AUC and C<sub>max</sub> Values**

Drug	Didanosine Dosage	n	% Change of Coadministered Drug Pharmacokinetic Parameters <sup>a</sup>	
			AUC of Coadministered Drug (95% CI)	C <sub>max</sub> of Coadministered Drug (95% CI)
ciprofloxacin, 750 mg every 12 hours for 3 days, 2 hours before didanosine	200 mg every 12 hours for 3 days	8 <sup>b</sup>	↓ 26%	↓ 16%
750 mg single dose	buffered placebo tablet	12	↓ 98%	↓ 93%

**Table 13: Results of Drug Interaction Studies with VIDEX: Effects of Didanosine on Coadministered Drug Plasma AUC and C<sub>max</sub> Values**

Drug	Didanosine Dosage	n	% Change of Coadministered Drug Pharmacokinetic Parameters <sup>a</sup>	
			AUC of Coadministered Drug (95% CI)	C <sub>max</sub> of Coadministered Drug (95% CI)
delavirdine, 400 mg single dose simultaneous 1 hour before didanosine	125 or 200 mg every 12 hours	12 <sup>b</sup>	↓ 32%	↓ 53%
	125 or 200 mg every 12 hours	12 <sup>b</sup>	↑ 20%	↑ 18%
ganciclovir, 1000 mg every 8 hours, 2 hours after didanosine	200 mg every 12 hours	12 <sup>b</sup>	↓ 21%	NA
indinavir, 800 mg single dose simultaneous 1 hour before didanosine	200 mg single dose	16	↓ 84%	↓ 82%
	200 mg single dose	16	↓ 11%	↓ 4%
ketoconazole, 200 mg/day for 4 days, 2 hours before didanosine	375 mg every 12 hours for 4 days	12 <sup>b</sup>	↓ 14%	↓ 20%
nelfinavir, 750 mg single dose, 1 hour after didanosine	200 mg single dose	10 <sup>b</sup>	↑ 12%	↔
dapsone, 100 mg single dose	200 mg every 12 hours for 14 days	6 <sup>b</sup>	↔	↔
ranitidine, 150 mg single dose, 2 hours before didanosine	375 mg single dose	12 <sup>b</sup>	↓ 16%	↔
ritonavir, 600 mg every 12 hours for 4 days	200 mg every 12 hours for 4 days	12	↔	↔
stavudine, 40 mg every 12 hours for 4 days	100 mg every 12 hours for 4 days	10 <sup>b</sup>	↔	↑ 17%
sulfamethoxazole, 1000 mg single dose	200 mg single dose	8 <sup>b</sup>	↓ 11% (-17, -4%)	↓ 12% (-28, 8%)
tenofovir, <sup>c</sup> 300 mg once daily 1 hour after didanosine	250 <sup>d</sup> or 400 mg once daily for 7 days	14	↔	↔
trimethoprim, 200 mg single dose	200 mg single dose	8 <sup>b</sup>	↑ 10% (-9, 34%)	↓ 22% (-59, 49%)
zidovudine, 200 mg every 8 hours for 3 days	200 mg every 12 hours for 3 days	6 <sup>b</sup>	↓ 10% (-27, 11%)	↓ 16.5% (-53, 47%)

↑ Indicates increase.

↓ Indicates decrease.

↔ Indicates no change, or mean increase or decrease of less than 10%.

<sup>a</sup> The 95% confidence intervals for the percent change in the pharmacokinetic parameter are displayed.

<sup>b</sup> HIV-infected patients.

**Table 13: Results of Drug Interaction Studies with VIDEX: Effects of Didanosine on Coadministered Drug Plasma AUC and C<sub>max</sub> Values**

Drug	Didanosine Dosage	n	% Change of Coadministered Drug Pharmacokinetic Parameters <sup>a</sup>	
			AUC of Coadministered Drug (95% CI)	C <sub>max</sub> of Coadministered Drug (95% CI)

<sup>c</sup> Tenofovir disoproxil fumarate.

<sup>d</sup> Patients less than 60 kg with creatinine clearance of at least 60 mL/min.

NA = Not available.

## 357 **12.4 Microbiology**

### 358 **Mechanism of Action**

359 Didanosine is a synthetic nucleoside analogue of the naturally occurring nucleoside  
 360 deoxyadenosine in which the 3'-hydroxyl group is replaced by hydrogen. Intracellularly,  
 361 didanosine is converted by cellular enzymes to the active metabolite, dideoxyadenosine  
 362 5'-triphosphate. Dideoxyadenosine 5'-triphosphate inhibits the activity of HIV-1 reverse  
 363 transcriptase both by competing with the natural substrate, deoxyadenosine  
 364 5'-triphosphate, and by its incorporation into viral DNA causing termination of viral  
 365 DNA chain elongation.

### 366 **Antiviral Activity in Cell Culture**

367 The anti-HIV-1 activity of didanosine was evaluated in a variety of HIV-1 infected  
 368 lymphoblastic cell lines and monocyte/macrophage cell cultures. The concentration of  
 369 drug necessary to inhibit viral replication by 50% (EC<sub>50</sub>) ranged from 2.5 to 10 μM  
 370 (1 μM = 0.24 μg/mL) in lymphoblastic cell lines and 0.01 to 0.1 μM in  
 371 monocyte/macrophage cell cultures.

### 372 **Resistance**

373 HIV-1 isolates with reduced sensitivity to didanosine have been selected in cell culture  
 374 and were also obtained from patients treated with didanosine. Genetic analysis of isolates

375 from didanosine-treated patients showed mutations in the reverse transcriptase gene that  
376 resulted in the amino acid substitutions K65R, L74V, and M184V. The L74V substitution  
377 was most frequently observed in clinical isolates. Phenotypic analysis of HIV-1 isolates  
378 from 60 patients (some with prior zidovudine treatment) receiving 6 to 24 months of  
379 didanosine monotherapy showed that isolates from 10 of 60 patients exhibited an average  
380 of a 10-fold decrease in susceptibility to didanosine in cell culture compared to baseline  
381 isolates. Clinical isolates that exhibited a decrease in didanosine susceptibility harbored  
382 one or more didanosine resistance-associated substitutions.

### 383 **Cross-resistance**

384 HIV-1 isolates from 2 of 39 patients receiving combination therapy for up to 2 years with  
385 didanosine and zidovudine exhibited decreased susceptibility to didanosine, lamivudine,  
386 stavudine, zalcitabine, and zidovudine in cell culture. These isolates harbored five  
387 substitutions (A62V, V75I, F77L, F116Y, and Q151M) in the reverse transcriptase gene.  
388 In data from clinical studies, the presence of thymidine analogue mutations (M41L,  
389 D67N, L210W, T215Y, K219Q) has been shown to decrease the response to didanosine.

## 390 **13 NONCLINICAL TOXICOLOGY**

### 391 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

392 Lifetime carcinogenicity studies were conducted in mice and rats for 22 and 24 months,  
393 respectively. In the mouse study, initial doses of 120, 800, and 1200 mg/kg/day for each  
394 sex were lowered after 8 months to 120, 210, and 210 mg/kg/day for females and 120,  
395 300, and 600 mg/kg/day for males. The two higher doses exceeded the maximally  
396 tolerated dose in females and the high dose exceeded the maximally tolerated dose in  
397 males. The low dose in females represented 0.68-fold maximum human exposure and the  
398 intermediate dose in males represented 1.7-fold maximum human exposure based on  
399 relative AUC comparisons. In the rat study, initial doses were 100, 250, and  
400 1000 mg/kg/day, and the high dose was lowered to 500 mg/kg/day after 18 months. The  
401 upper dose in male and female rats represented 3-fold maximum human exposure.

402 Didanosine induced no significant increase in neoplastic lesions in mice or rats at  
403 maximally tolerated doses.

404 Didanosine was positive in the following genetic toxicology assays: 1) the *Escherichia*  
405 *coli* tester strain WP2 uvrA bacterial mutagenicity assay; 2) the L5178Y/TK+/- mouse  
406 lymphoma mammalian cell gene mutation assay; 3) the *in vitro* chromosomal aberrations  
407 assay in cultured human peripheral lymphocytes; 4) the *in vitro* chromosomal aberrations  
408 assay in Chinese Hamster Lung cells; and 5) the BALB/c 3T3 *in vitro* transformation  
409 assay. No evidence of mutagenicity was observed in an Ames *Salmonella* bacterial  
410 mutagenicity assay or in rat and mouse *in vivo* micronucleus assays.

## 411 **13.2 Animal Toxicology and/or Pharmacology**

412 Evidence of a dose-limiting skeletal muscle toxicity has been observed in mice and rats  
413 (but not in dogs) following long-term (greater than 90 days) dosing with didanosine at  
414 doses that were approximately 1.2 to 12 times the estimated human exposure. The  
415 relationship of this finding to the potential of VIDEX (didanosine) to cause myopathy in  
416 humans is unclear. However, human myopathy has been associated with administration  
417 of VIDEX and other nucleoside analogues.

## 418 **14 CLINICAL STUDIES**

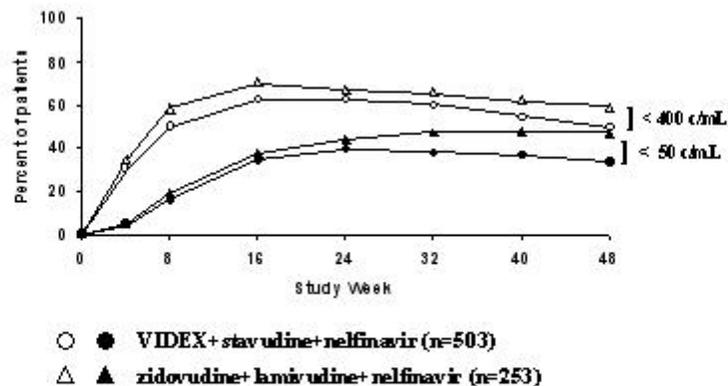
### 419 **14.1 Adult Patients**

#### 420 **Combination Therapy**

421 START 2 was a multicenter, randomized, open-label study comparing VIDEX (200 mg  
422 twice daily)/stavudine/indinavir to zidovudine/lamivudine/indinavir in 205 treatment-  
423 naive patients. Both regimens resulted in a similar magnitude of suppression of HIV-1  
424 RNA levels and increases in CD4 cell counts through 48 weeks.

425 Study A1454-148 was a randomized, open-label, multicenter study comparing treatment  
426 with VIDEX (400 mg once daily) plus stavudine (40 mg twice daily) and nelfinavir  
427 (750 mg three times daily) versus zidovudine (300 mg twice daily) plus lamivudine  
428 (150 mg twice daily) and nelfinavir (750 mg three times daily) in 756 treatment-naive  
429 patients, with a median CD4 cell count of 340 cells/mm<sup>3</sup> (range 80 to 1568 cells/mm<sup>3</sup>)  
430 and a median plasma HIV-1 RNA of 4.69 log<sub>10</sub> copies/mL (range 2.6 to 5.9 log<sub>10</sub>  
431 copies/mL) at baseline. Median CD4 cell count increases at 48 weeks were  
432 188 cells/mm<sup>3</sup> in both treatment groups. Treatment response and outcomes through  
433 48 weeks are shown in Figure 1 and Table 14.

**Figure 1: Treatment Response Through Week 48\*, AI454-148**



\* Percent of patients at each time point who have HIV RNA <400 or <50 copies/mL, are on their original study medication (except stavudine-zidovudine switches), and have not experienced an AIDS-defining event.

434

**Table 14: Outcomes of Randomized Treatment Through Week 48, AI454-148**

Week 48 Status	Percent of Patients with HIV RNA less than 400 copies/mL (less than 50 copies/mL)	
	VIDEX/stavudine/nelfinavir n=503	lamivudine/zidovudine/nelfinavir n=253
Responder <sup>a</sup>	50* (34*)	59 (47)
Virologic failure <sup>b</sup>	36 (57)	32 (48)
Death or disease progression	less than 1 (less than 1)	1 (less than 1)
Discontinued due to adverse events	4 (2)	2 (less than 1)
Discontinued due to other reasons <sup>c</sup>	6 (3)	4 (2)
Never initiated treatment	4 (4)	2 (2)

\* p less than 0.05 for the differences between treatment groups, by Cochran-Mantel-Haenszel test.

<sup>a</sup> Patients achieved virologic response [two consecutive viral loads less than 400 (less than 50) copies/mL] and maintained it to Week 48.

<sup>b</sup> Includes viral rebound and failing to achieve confirmed less than 400 (less than 50) copies/mL by Week 48.

<sup>c</sup> Includes lost to follow-up, noncompliance, withdrawal, and pregnancy.

435 **Monotherapy**

436 The efficacy of VIDEX was demonstrated in two randomized, double-blind studies  
437 comparing VIDEX, given on a twice-daily schedule, to zidovudine, given three times  
438 daily, in 617 (ACTG 116A, conducted 1989-1992) and 913 (ACTG 116B/117, conducted  
439 1989-1991) patients with symptomatic HIV infection or AIDS who were treated for more  
440 than one year. In treatment-naive patients (ACTG 116A), the rate of HIV disease  
441 progression or death was similar between the treatment groups; mortality rates were 26%  
442 for patients receiving VIDEX and 21% for patients receiving zidovudine. Of the patients  
443 who had received previous zidovudine treatment (ACTG 116B/117), those treated with  
444 VIDEX had a lower rate of HIV disease progression or death (32%) compared to those  
445 treated with zidovudine (41%); however, survival rates were similar between the  
446 treatment groups.

447 Studies have demonstrated that the clinical benefit of monotherapy with antiretrovirals,  
448 including VIDEX, was time limited.

449 **14.2 Pediatric Patients**

450 Efficacy in pediatric patients was demonstrated in a randomized, double-blind, controlled  
451 study (ACTG 152, conducted 1991-1995) involving 831 patients 3 months to 18 years of  
452 age treated for more than 1.5 years with zidovudine (180 mg/m<sup>2</sup> every 6 hours), VIDEX  
453 (120 mg/m<sup>2</sup> every 12 hours), or zidovudine (120 mg/m<sup>2</sup> every 6 hours) plus VIDEX  
454 (90 mg/m<sup>2</sup> every 12 hours). Patients treated with VIDEX or VIDEX plus zidovudine had  
455 lower rates of HIV-1 disease progression or death compared with those treated with  
456 zidovudine alone.

457 **16 HOW SUPPLIED/STORAGE AND HANDLING**

458 VIDEX (didanosine, USP) Pediatric Powder for Oral Solution is supplied as shown in  
459 Table 15:

**Table 15: VIDEX Pediatric Powder for Oral Solution**

NDC NO.	Packaging Information	Product Quantity
0087-6632-41	One, 4-ounce glass, bottle per carton	2 g/bottle
0087-6633-41	One, 8-ounce glass, bottle per carton	4 g/bottle

460 Prior to dispensing, the pharmacist must reconstitute dry powder with Purified Water,  
461 USP, to an initial concentration of 20 mg/mL and immediately mix the resulting solution  
462 with antacid to a final concentration of 10 mg/mL as follows:

463 **20 mg/mL Initial Solution**

464 Reconstitute the product to 20 mg/mL by adding 100 mL or 200 mL of Purified Water,  
465 USP, to the 2 g or 4 g of VIDEX powder, respectively, in the product bottle.

466 **10 mg/mL Final Admixture**

- 467 1. Immediately mix one part of the 20 mg/mL initial solution with one part of Maximum  
468 Strength Mylanta<sup>®</sup> Liquid for a final dispensing concentration of 10 mg VIDEX per  
469 mL. For patient home use, the admixture should be dispensed in appropriately sized,  
470 flint-glass or plastic (HDPE, PET, or PETG) bottles with child-resistant closures.
- 471 2. Instruct the patient to shake the admixture thoroughly prior to use and to store the  
472 tightly closed container in the refrigerator.

473 **Storage**

474 The bottles of powder should be stored at 59° F to 86° F (15° C to 30° C). The VIDEX  
475 admixture may be stored up to 30 days in a refrigerator, 36° F to 46° F (2° C to 8° C).  
476 Discard any unused portion after 30 days.

477 \_\_\_\_\_

478 Mylanta<sup>®</sup> is a registered trademark of Johnson & Johnson-Merck Consumer  
479 Pharmaceuticals Company.

480 **17 PATIENT COUNSELING INFORMATION**

481 *See FDA-approved Patient Labeling (17.6)*

482 **17.1 Pancreatitis**

483 Patients should be informed that a serious toxicity of VIDEX, used alone and in  
484 combination regimens, is pancreatitis, which may be fatal.

485 **17.2 Peripheral Neuropathy**

486 Patients should be informed that peripheral neuropathy, manifested by numbness,  
487 tingling, or pain in hands or feet, may develop during therapy with VIDEX. Patients  
488 should be counseled that peripheral neuropathy occurs with greatest frequency in patients  
489 with advanced HIV-1 disease or a history of peripheral neuropathy, and that  
490 discontinuation of VIDEX may be required if toxicity develops.

491 **17.3 Lactic Acidosis and Severe Hepatomegaly with**  
492 **Steatosis**

493 Patients should be informed that lactic acidosis and severe hepatomegaly with steatosis,  
494 including fatal cases, have been reported with the use of nucleoside analogues alone or in  
495 combination, including didanosine and other antiretrovirals.

496 **17.4 Hepatic Toxicity**

497 Patients should be informed that hepatotoxicity including fatal hepatic adverse events  
498 were reported in patients with preexisting liver dysfunction. The safety and efficacy of  
499 VIDEX have not been established in HIV-infected patients with significant underlying  
500 liver disease.

501 **17.5 Retinal Changes and Optic Neuritis**

502 Patients should be informed that retinal changes and optic neuritis have been reported in  
503 adult and pediatric patients.

504 **17.6 Fat Redistribution**

505 Patients should be informed that redistribution or accumulation of body fat may occur in  
506 patients receiving antiretroviral therapy and that the cause and long-term health effects of  
507 these conditions are not known at this time.

508 **17.7 Concomitant Therapy**

509 Patients should be informed that when VIDEX is used in combination with other agents  
510 with similar toxicities, the incidence of adverse events may be higher than when VIDEX  
511 is used alone. These patients should be followed closely.

512 Patients should be cautioned about the use of medications or other substances, including  
513 alcohol, which may exacerbate VIDEX toxicities.

514 **17.8 General Information**

515 VIDEX (didanosine) is not a cure for HIV-1 infection, and patients may continue to  
516 develop HIV-associated illnesses, including opportunistic infection. Therefore, patients  
517 should remain under the care of a physician when using VIDEX. Patients should be  
518 advised that VIDEX therapy has not been shown to reduce the risk of transmission of  
519 HIV to others through sexual contact or blood contamination. Patients should be  
520 informed that the long-term effects of VIDEX are unknown at this time.

521 Patients should be informed that the preferred dosing frequency of VIDEX is twice daily  
522 because there is more evidence to support the effectiveness of this dosing frequency.  
523 Once-daily dosing should be considered only for patients whose management requires  
524 once-daily dosing of VIDEX.

525 **17.9 FDA-Approved Patient Labeling**

526 **VIDEX<sup>®</sup>**

527 (generic name = **didanosine** also known as **ddI**)

528 VIDEX<sup>®</sup> (didanosine, USP) Pediatric Powder for Oral Solution

529 **What is VIDEX?**

530 VIDEX (pronounced *VY dex*) is a prescription medicine used in combination with other  
531 drugs to treat children and adults who are infected with HIV (the human  
532 immunodeficiency virus, the virus that causes AIDS). VIDEX belongs to a class of drugs  
533 called nucleoside analogues. By reducing the growth of HIV, VIDEX helps your body  
534 maintain its supply of CD4 cells, which are important for fighting HIV and other  
535 infections.

536 VIDEX will not cure your HIV infection. At present there is no cure for HIV infection.  
537 Even while taking VIDEX, you may continue to have HIV-related illnesses, including  
538 infections with other disease-producing organisms. Continue to see your doctor regularly  
539 and report any medical problems that occur.

540 VIDEX does not prevent a patient infected with HIV from passing the virus to other  
541 people. To protect others, you must continue to practice safe sex and take precautions to  
542 prevent others from coming in contact with your blood and other body fluids.

543 There is limited information on the effects of long-term use of VIDEX.

544 **Who should not take VIDEX?**

545 Do not take VIDEX if you are allergic to any of its ingredients, including its active  
546 ingredient, didanosine, and the inactive ingredients. (See *Inactive Ingredients* at the end  
547 of this leaflet.) Tell your doctor if you think you have had an allergic reaction to any of  
548 these ingredients.

549 **How should I take VIDEX? How should I store it?**

550 Your doctor will determine your dose based on your body weight, kidney and liver  
551 function, other medicines you are taking, and any side effects that you may have had with  
552 VIDEX or other medicines. Take VIDEX **on an empty stomach - that means at least**  
553 **30 minutes before or 2 hours after eating. Do not take VIDEX with food.** Try not to  
554 miss a dose, but if you do, take it as soon as possible. If it is almost time for the next  
555 dose, skip the missed dose and continue your regular dosing schedule.

556 Your pharmacist will prepare the oral solution. Shake the solution well before each  
557 use. Store in the refrigerator. Throw away any unused portion after 30 days.

558 **If you have kidney disease:** If your kidneys are not working properly, your doctor will  
559 need to do regular tests to check how they are working while you take VIDEX. Your  
560 doctor may also lower your dosage of VIDEX.

561 **What should I do if someone takes an overdose of VIDEX?**

562 If someone may have taken an overdose of VIDEX, get medical help right away. Contact  
563 their doctor or a poison control center.

564 **What should I avoid while taking VIDEX?**

565 **Alcohol.** Do not drink alcohol while taking VIDEX since alcohol may increase your risk  
566 of pancreatitis (pain and inflammation of the pancreas) or liver damage.

567 **Allopurinol**, also known as ZYLOPRIM<sup>®</sup>, ALOPRIM<sup>®</sup>, or others. Do not take  
568 allopurinol while taking VIDEX because the risk of side-effects of didanosine are  
569 increased.

570 **Ribavirin**, also known as COPEGUS<sup>®</sup>, REBETOL<sup>®</sup>, or others. Do not take ribavirin  
571 while taking VIDEX because pancreatitis, peripheral neuropathy, lactic acidosis and fatal  
572 liver damage have been reported. (See "What are the possible side effects of VIDEX?")

573 **Other medicines.** Other medicines, including those you can buy without a prescription,  
574 may interfere with the actions of VIDEX or may increase the possibility or severity of

575 side effects. **Do not take any medicine, vitamin supplement, or other health**  
576 **preparation without first checking with your doctor.**

577 **Antacids.** Since VIDEX is mixed with an antacid, any side effects related to  
578 VIDEX's ingredients may get worse if you also take an antacid.

579 **Medicines at the same time you take your VIDEX dose.** Some medicines should  
580 not be taken at the same time of day that you take VIDEX. Check with your doctor.

581 **Pregnancy.** It is not known if VIDEX can harm a human fetus. Also, pregnant women  
582 have experienced serious side effects when taking VIDEX in combination with ZERIT  
583 (stavudine), also known as d4T, and other HIV medicines. VIDEX should be used during  
584 pregnancy only after discussion with your doctor. **Tell your doctor if you become**  
585 **pregnant or plan to become pregnant while taking VIDEX.**

586 **Nursing.** Studies have shown VIDEX is in the breast milk of animals getting the drug. It  
587 may also be in human breast milk. The Centers for Disease Control and Prevention  
588 (CDC) recommends that HIV-infected mothers **not** breast-feed. This should reduce the  
589 risk of passing HIV infection to their babies and the potential for serious adverse  
590 reactions in nursing infants. Therefore, do not nurse a baby while taking VIDEX.

591 **What are the possible side effects of VIDEX?**

592 **Pancreatitis.** Pancreatitis is a dangerous inflammation of the pancreas that may cause  
593 death. *Tell your doctor right away if you or a child taking VIDEX develops stomach*  
594 *pain, nausea, or vomiting. These can be signs of pancreatitis.* Before starting VIDEX  
595 therapy, let your doctor know if you or a child for whom it has been prescribed has ever  
596 had pancreatitis. This condition is more likely to happen in people who have had it  
597 before. It is also more likely in people with advanced HIV disease. However, it can occur  
598 at any stage of HIV disease. It may be more common in patients with kidney problems,  
599 those who drink alcohol, and those who are also treated with stavudine. If you get  
600 pancreatitis, your doctor will tell you to stop taking VIDEX.

601 **Lactic acidosis, severe liver enlargement, and liver failure**, including deaths, have  
602 been reported among patients taking VIDEX (including pregnant women). Symptoms  
603 that may indicate a liver problem are:

- 604 • feeling very weak, tired, or uncomfortable
- 605 • unusual or unexpected stomach discomfort
- 606 • feeling cold
- 607 • feeling dizzy or lightheaded
- 608 • suddenly developing a slow or irregular heartbeat

609 **Lactic acidosis is a medical emergency that must be treated in a hospital.**

610 If you notice any of these symptoms or if your medical condition changes, stop taking  
611 VIDEX and **call your doctor right away**. Women, overweight patients, and those who  
612 have been treated for a long time with other medicines used to treat HIV infection are  
613 more likely to develop lactic acidosis. Your doctor should check your liver function  
614 periodically while you are taking VIDEX. You should be especially careful if you have a  
615 history of heavy alcohol use or a liver problem.

616 **Vision changes.** VIDEX (didanosine) may affect the nerves in your eyes. Because of  
617 this, you should have regular eye examinations. You should also report any changes in  
618 vision to your doctor right away. This includes, for example, seeing colors abnormally or  
619 blurred vision.

620 **Peripheral neuropathy.** This is a problem with the nerves in your hands or feet. The  
621 nerve problem may be serious. ***Tell your doctor right away if you or a child taking***  
622 ***VIDEX has continuing numbness, tingling, or pain in the feet or hands.*** A child may  
623 not recognize these symptoms or know to tell you that his or her feet or hands are numb,  
624 burning, tingling, or painful. Ask your child's doctor how to find out if your child is  
625 developing peripheral neuropathy.

626 Before starting VIDEX therapy, let your doctor know if you or a child for whom it has  
627 been prescribed has ever had peripheral neuropathy. This condition is more likely to  
628 happen in people who have had it before. It is also more likely in patients taking  
629 medicines that affect the nerves and in people with advanced HIV disease. However, it  
630 can occur at any stage of HIV disease. If you get peripheral neuropathy, your doctor will  
631 tell you to stop taking VIDEX. After stopping VIDEX, the symptoms may get worse for

632 a short time and then get better. Once symptoms of peripheral neuropathy go away  
633 completely, you and your doctor should decide if starting VIDEX again is right for you.

634 **Special note about other medicines.** If you take VIDEX along with other medicines  
635 with similar side effects, you may increase the chance of having these side effects. For  
636 example, using VIDEX in combination with other medicines that may cause pancreatitis,  
637 peripheral neuropathy, or liver problems (including stavudine) may increase your chance  
638 of having these side effects.

639 **Other side effects:** The most common side effects in adults taking VIDEX in  
640 combination with other HIV drugs included diarrhea, neuropathy (nerve disorders), chills  
641 or fever, rash, abdominal pain, weakness, headache, and nausea and vomiting. Children  
642 may have similar side effects as adults.

643 Changes in body fat have been seen in some patients taking antiretroviral therapy. These  
644 changes may include an increased amount of fat in the upper back and neck (“buffalo  
645 hump”), breast, and around the trunk. Loss of fat from the legs, arms, and face may also  
646 happen. The cause and long-term health effects of these conditions are not known at this  
647 time.

#### 648 **Inactive Ingredients:**

649 **Pediatric Oral Solution:** Maximum Strength Mylanta<sup>®</sup> Liquid.

650

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651 This medicine was prescribed for your particular condition. Do not use VIDEX for  
652 another condition or give it to others. Keep all medicines out of the reach of children and  
653 pets at all times. Do not keep medicine that is out of date or that you no longer need.  
654 Dispose of unused medicines through community take-back disposal programs when  
655 available or place VIDEX in an unrecognizable closed container in the household trash.

656 This summary does not include everything there is to know about VIDEX. Medicines are  
657 sometimes prescribed for purposes other than those listed in a Patient Information  
658 Leaflet. If you have questions or concerns, or want more information about VIDEX, your  
659 physician and pharmacist have the complete prescribing information upon which this  
660 leaflet is based. You may want to read it and discuss it with your doctor or other  
661 healthcare professional. Remember, no written summary can replace careful discussion  
662 with your doctor.

663 VIDEX<sup>®</sup> and Zerit<sup>®</sup> are registered trademarks of Bristol-Myers Squibb Company. All  
664 other trademarks are the property of their respective owners.

665 Bristol-Myers Squibb Company  
666 Princeton, NJ 08543 USA

667 This Patient Information Leaflet has been approved by the U.S. Food and Drug  
668 Administration.

669 XXXXXXXX

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