VIDEX® EC
(didanosine)

Rx only

VIDEX® EC (didanosine) Delayed-Release Capsules Enteric-Coated Beadlets

(Patient Information Leaflet Included)

WARNING

FATAL AND NONFATAL PANCREATITIS HAVE OCCURRED DURING THERAPY WITH DIDANOSINE USED ALONE OR IN COMBINATION REGIMENS IN BOTH TREATMENT-NAIVE AND TREATMENT-EXPERIENCED PATIENTS, REGARDLESS OF DEGREE OF IMMUNOSUPPRESSION. VIDEX EC SHOULD BE SUSPENDED IN PATIENTS WITH SUSPECTED PANCREATITIS AND DISCONTINUED IN PATIENTS WITH CONFIRMED PANCREATITIS (SEE WARNINGS).

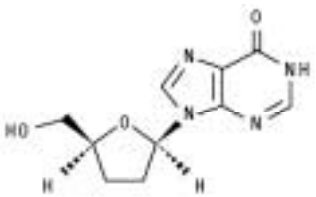
LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS, INCLUDING FATAL CASES, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGUES ALONE OR IN COMBINATION, INCLUDING DIDANOSINE AND OTHER ANTIRETROVIRALS. FATAL LACTIC ACIDOSIS HAS BEEN REPORTED IN PREGNANT WOMEN WHO RECEIVED THE COMBINATION OF DIDANOSINE 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: PREGNANCY.)

DESCRIPTION

VIDEX® EC is the brand name for an enteric-coated formulation of didanosine (ddI), a synthetic purine nucleoside analogue active against the Human Immunodeficiency Virus (HIV). VIDEX EC (didanosine) Delayed-Release Capsules, containing enteric-coated beadlets, are available for oral administration in strengths of 125, 200, 250, and 400 mg of didanosine. The inactive ingredients in the beadlets include carboxymethylcellulose sodium 12, diethyl phthalate, methacrylic acid copolymer, sodium hydroxide, sodium starch glycolate, and talc. The capsule shells contain colloidal silicon dioxide, gelatin, sodium lauryl sulfate, and titanium dioxide. The capsules are imprinted with edible inks.

Didanosine is also available as buffered formulations. Please consult the prescribing information for VIDEX (didanosine) buffered formulations and Pediatric Powder for Oral Solution for additional information.

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



Didanosine is a white crystalline powder with the molecular formula $C_{10}H_{12}N_4O_3$ and a molecular weight of 236.2. The aqueous solubility of didanosine at 25° C and pH of approximately 6 is 27.3 mg/mL. Didanosine is unstable in acidic solutions. For example, at pH <3 and 37° C, 10% of didanosine decomposes to hypoxanthine in less than 2 minutes. In VIDEX EC, an enteric coating is used to protect didanosine from degradation by stomach acid.

MICROBIOLOGY

Mechanism of Action

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

In Vitro HIV Susceptibility

The *in vitro* anti-HIV-1 activity of didanosine was evaluated in a variety of HIV-1 infected lymphoblastic cell lines and monocyte/macrophage cell cultures. The concentration of drug necessary to inhibit viral replication by 50% (IC_{50}) ranged from 2.5 to 10 μM (1 μM = 0.24 μg/mL) in lymphoblastic cell lines and 0.01 to 0.1 μM in monocyte/macrophage cell cultures. The relationship between *in vitro* susceptibility of HIV to didanosine and the inhibition of HIV replication in humans has not been established.

Drug Resistance

HIV-1 isolates with reduced sensitivity to didanosine have been selected *in vitro* and were also obtained from patients treated with didanosine. Genetic analysis of isolates from didanosine-treated patients showed mutations in the reverse transcriptase gene that resulted in the amino acid substitutions K65R, L74V, and M184V. The L74V mutation was most frequently observed in clinical isolates. Phenotypic analysis of HIV-1 isolates from 60 patients (some with prior zidovudine treatment) receiving 6 to 24 months of didanosine monotherapy showed that isolates from 10 of 60 patients exhibited an average of a 10-fold decrease in susceptibility to didanosine *in vitro* compared to baseline isolates. Clinical isolates that exhibited a decrease in didanosine susceptibility harbored one or more didanosine-associated mutations. The clinical relevance of genotypic and phenotypic changes associated with didanosine therapy has not been established.

Cross-resistance

HIV-1 isolates from 2 of 39 patients receiving combination therapy for up to 2 years with zidovudine and didanosine exhibited decreased susceptibility to zidovudine, didanosine, zalcitabine, stavudine, and lamivudine *in vitro*. These isolates harbored five mutations (A62V, V75I, F77L, F116Y, and Q151M) in the reverse transcriptase gene. The clinical relevance of these observations has not been established.

CLINICAL PHARMACOLOGY

Animal Toxicology

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

Pharmacokinetics

The pharmacokinetic parameters of didanosine are summarized in Table 1. Didanosine is rapidly absorbed, with peak plasma concentrations generally observed from 0.25 to 1.50 hours following oral dosing with a buffered formulation. Increases in plasma didanosine concentrations were dose proportional over the range of 50 to 400 mg. Steady-state pharmacokinetic parameters did not differ significantly from values obtained after a single dose. Binding of didanosine to plasma proteins *in vitro* was low (<5%). Based on data from *in vitro* and animal studies, it is presumed that the metabolism of didanosine in man occurs by the same pathways responsible for the elimination of endogenous purines.

Table 1
Pharmacokinetic Parameters for Didanosine in Adults

Parameter	Mean ± SD	n
Oral bioavailability[a]	42 ± 12%	6
Apparent volume of distribution[b]	1.08 ± 0.22 L/kg	6
CSF-plasma ratio[b]	21 ± 0.03%[c]	5
Systemic clearance[b]	13.0 ± 1.6 mL/min/kg	6
Renal clearance[a]	5.5 ± 2.1 mL/min/kg	6
Elimination half-life[a]	1.5 ± 0.4 h	6
Urinary recovery of didanosine[a]	18 ± 8%	6

CSF = cerebrospinal fluid.
[a] following oral administration of a buffered formulation.
[b] following IV administration.
[c] mean ± SE.

Comparison of Didanosine Formulations

In VIDEX EC, the active ingredient, didanosine, is protected against degradation by stomach acid by the use of an enteric coating on the beadlets in the capsule. The enteric coating dissolves when the beadlets empty into the small intestine, the site of drug absorption. With buffered formulations of didanosine, administration with antacid provides protection from degradation by stomach acid.

In healthy volunteers, as well as subjects infected with HIV, the area under the plasma concentration time curve (AUC) is equivalent for didanosine administered as the VIDEX EC formulation relative to a buffered tablet formulation. The peak plasma concentration (C_{MAX}) of didanosine, administered as VIDEX EC, is reduced approximately 40% relative to didanosine buffered tablets. The time to the peak concentration (T_{MAX}) increases from approximately 0.67 hours for didanosine buffered tablets to 2.0 hours for VIDEX EC.

Effect of Food on Absorption of Didanosine

In the presence of food, the C_{MAX} and AUC for VIDEX EC were reduced by approximately 46% and 19%, respectively, compared to the fasting state. VIDEX EC should be taken on an empty stomach.

Special Populations

Renal Insufficiency

It is recommended that the VIDEX EC (didanosine) dose be modified in patients with reduced creatinine clearance and in patients receiving maintenance hemodialysis (see **DOSAGE AND ADMINISTRATION**). Data from two studies using a buffered formulation of didanosine indicated that the apparent oral clearance of didanosine decreased and the terminal elimination half-life increased as creatinine clearance decreased (see Table 2). Following oral administration, didanosine was not detectable in peritoneal dialysate fluid (n=6); recovery in hemodialysate (n=5) ranged from 0.6% to 7.4% of the dose over a 3-4 hour dialysis period. The absolute bioavailability of didanosine was not affected in patients requiring dialysis.

Table 2
Mean ± SD Pharmacokinetic Parameters for Didanosine Following a Single Oral Dose of a Buffered Formulation

	Creatinine Clearance (mL/min)				
Parameter	≥ 90 (n=12)	60-90 (n=6)	30-59 (n=6)	10-29 (n=3)	Dialysis Patients (n=11)
CL_{cr} (mL/min)	112±22	68±8	46±8	13±5	ND[a]
CL/F (mL/min)	2164±638	1566±833	1023±378	628±104	543±174
CL_R (mL/min)	458±164	247±153	100±44	20±8	<10
$T_{1/2}$ (h)	1.42±0.33	1.59±0.13	1.75±0.43	2.0±0.3	4.1±1.2

[a]ND = not determined due to anuria.
CL_{cr} = creatinine clearance.
CL/F = apparent oral clearance.
CL_R = renal clearance.

Pediatric Patients

The pharmacokinetics of didanosine administered as VIDEX EC have not been studied in pediatric patients.

Geriatric Patients

Didanosine pharmacokinetics have not been studied in patients over 65 years of age (see **PRECAUTIONS: Geriatric Use**).

Gender

The effects of gender on didanosine pharmacokinetics have not been studied.

Drug Interactions (See also **PRECAUTIONS: Drug Interactions**.)

VIDEX EC

Table 3 summarizes the effects of coadministration of VIDEX EC (didanosine) on the AUC and C_{MAX} of ciprofloxacin, indinavir, and ketoconazole. No clinically significant pharmacokinetic interactions were observed between this formulation of didanosine and these agents.

Table 3
Results of Drug Interaction Studies with VIDEX EC: Effects of Didanosine on Coadministered Drug Plasma AUC and C_{MAX} Values*

Drug	Didanosine Dosage	n	AUC of Coadministered Drug	C_{MAX} of Coadministered Drug
ciprofloxacin, 750 mg single dose	400 mg single dose	16	↔	↔
indinavir, 800 mg single dose	400 mg single dose	23	↔	↔
ketoconazole, 200 mg single dose	400 mg single dose	21	↔	↔

↔indicates no change, or mean increase or decrease of <10%.
*All studies conducted in healthy volunteers.

Didanosine Buffered Formulations

Tables 4 and 5 summarize the effects on AUC and C_{MAX}, with a 90% or 95% confidence interval (CI) when available, following coadministration of buffered formulations of didanosine with a variety of drugs. Except as noted in table footnotes, the results of these studies may be expected to apply to VIDEX EC. For most of the listed drugs, no clinically significant pharmacokinetic interactions were observed. Clinical recommendations based on drug interaction studies for drugs in bold font are included in **PRECAUTIONS: Drug Interactions.**

Table 4
Results of Drug Interaction Studies with Buffered Formulations of Didanosine: Effects of Coadministered Drug on Didanosine Plasma AUC and C_{MAX} Values

Drug	Didanosine Dosage	n	AUC of Didanosine (95% CI)	C_{MAX} of Didanosine (95% CI)
***Drugs With Clinical Recommendations Regarding Coadministration (see* PRECAUTIONS: Drug Interactions)**				
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%
ganciclovir, 1000 mg q8h, 2 h after didanosine	200 mg q12h	12	↑111%	NA
methadone, chronic maintenance dose	200 mg single dose	16, 10[a]	↓ 41%	↓ 59%
No Clinically Significant Interaction Observed				
Drug	**Didanosine Dosage**	**n**	**AUC of Didanosine (95% CI)**	**C_{MAX} of Didanosine (95% CI)**
ciprofloxacin, 750 mg q12h for 3 days, 2 h before didanosine	200 mg q12h for 3 days	8[b]	↓ 16%	↓ 28%
indinavir, 800 mg single dose simultaneous	200 mg single dose	16	↔	↔
1 h before didanosine	200 mg single dose	16	↓17% (-27, -7%)[c]	↓13% (-28, 5%)[c]
ketoconazole, 200 mg/day for 4 days, 2 h before didanosine	375 mg q12h for 4 days	12[b]	↔	↓ 12%
loperamide, 4 mg q6h for 1 day	300 mg single dose	12[b]	↔	↓ 23%
metoclopramide, 10 mg single dose	300 mg single dose	12[b]	↔	↑ 13%
ranitidine, 150 mg single dose, 2 h before didanosine	375 mg single dose	12[b]	↑ 14%	↑ 13%
rifabutin, 300 or 600 mg/day for 12 days	167 or 250 mg q12h for 12 days	11	↑13% (-1, 27%)	↑17% (-4, 38%)
ritonavir, 600 mg q12h for 4 days	200 mg q12h for 4 days	12	↓13% (0, 23%)	↓16% (5, 26%)
stavudine, 40 mg q12h for 4 days	100 mg q12h for 4 days	10	↔	↔
sulfamethoxazole, 1000 mg single dose	200 mg single dose	8[b]	↔	↔
trimethoprim, 200 mg single dose	200 mg single dose	8[b]	↔	↑17% (-23, 77%)
zidovudine, 200 mg q8h for 3 days	200 mg q12h for 3 days	6[b]	↔	↔

↑indicates increase.
↓indicates decrease.
↔indicates no change, or mean increase or decrease of <10%.
[a]Parallel-group design; entries are subjects receiving combination and control regimens, respectively.
[b]HIV-infected patients.
[c]90% CI.
NA Not available.

Table 5
Results of Drug Interaction Studies with Buffered Formulations of Didanosine: Effects of Didanosine on Coadministered Drug Plasma AUC and C_{MAX} Values

Drug	Didanosine Dosage	n	AUC of Coadministered Drug (95% CI)	C_{MAX} of Coadministered Drug (95% CI)
No Clinically Significant Interaction Observed				
dapsone, 100 mg single dose	200 mg q12h for 14 days	6[a]	↔	↔
delavirdine, 400 mg single dose simultaneous	125 or 200 mg q12h	12[a]	↓32%[b]	↓53%[b]
1 h before didanosine	125 or 200 mg q12h	12[a]	↑20%	↑18%
ganciclovir, 1000 mg q8h, 2 h after didanosine	200 mg q12h	12[a]	↓21%	NA
nelfinavir, 750 mg single dose, 1 h after didanosine	200 mg single dose	10[a]	↑12%	↔
ranitidine, 150 mg single dose, 2 h before didanosine	375 mg single dose	12[a]	↓16%	↔
ritonavir, 600 mg q12h for 4 days	200 mg q12h for 4 days	12	↔	↔
stavudine, 40 mg q12h for 4 days	100 mg q12h for 4 days	10[a]	↔	↑17%
sulfamethoxazole, 1000 mg single dose	200 mg single dose	8[a]	↓11% (-17, -4%)	↓12% (-28, 8%)
trimethoprim, 200 mg single dose	200 mg single dose	8[a]	↑10% (-9, 34%)	↓22% (-59, 49%)
zidovudine, 200 mg q8h for 3 days	200 mg q12h for 3 days	6[a]	↓10% (-27, 11%)	↓16.5% (-53, 47%)

↑indicates increase.
↓indicates decrease.
↔indicates no change, or mean increase or decrease of <10%.
[a]HIV-infected patients.
[b]This result is probably related to the buffer and is not expected to occur with VIDEX EC.
NA Not available.

INDICATIONS AND USAGE

VIDEX EC (didanosine) in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection in adults whose management requires once-daily administration of didanosine or an alternative didanosine formulation. (See **Clinical Studies, PRECAUTIONS: Frequency of Dosing,** and **DOSAGE AND ADMINISTRATION**.)

There are limited data to date to support the long-term durability of response with a once-daily dosing regimen of didanosine.

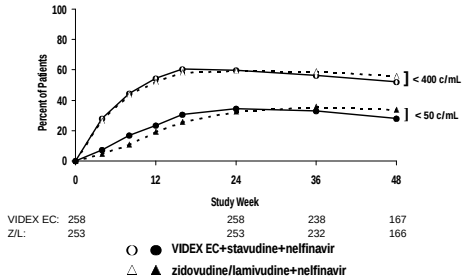
Clinical Studies

Once-daily dosing of didanosine produces a pharmacokinetic profile that is substantially different from that observed with twice-daily dosing of didanosine (see **CLINICAL PHARMACOLOGY**). Further, VIDEX EC and the VIDEX (didanosine) buffered formulation produce substantially different pharmacokinetic profiles when dosed once daily. Therefore, controlled clinical trials were conducted with both formulations to evaluate the safety and efficacy of once-daily dosing of didanosine. There is no evaluable long-term clinical information that directly compares the efficacy of the two once-daily didanosine formulations. A small clinical study that was conducted to address this issue was not interpretable due to the small number of patients who completed the study.

Once-Daily VIDEX EC Study

Study AI454-152 is an ongoing, 48-week, randomized, open-label study comparing VIDEX EC (400 mg once daily) plus stavudine (40 mg twice daily) plus nelfinavir (750 mg three times daily) to zidovudine (200 mg twice daily) plus lamivudine (150 mg twice daily) combination tablets plus nelfinavir (750 mg three times daily) in 511 treatment-naive patients, with a mean CD4 cell count of 411 cells/mm^3 (range 39 to 1105 cells/mm^3) and a mean plasma HIV-1 RNA of 4.71 $\log_{10}$ copies/mL (range 2.8 to 5.9 $\log_{10}$ copies/mL) at baseline. Patients were primarily males (72%) and Caucasian (53%) with a mean age of 35 years (range 18 to 73 years). The percentages of patients with HIV RNA <400 and <50 copies/mL and not meeting any criteria for treatment failure (eg, virologic failure, discontinuation for any reason, or AIDS-defining event) through 48 weeks are shown in Figure 1.

Figure 1
Treatment Response Through Week 48*, AI454-152



VIDEX EC:	258	258	238	167
Z/L:	253	253	232	166

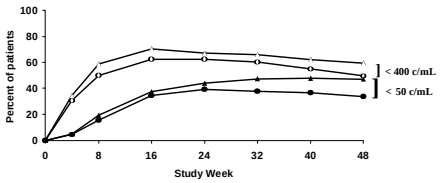
○ ● VIDEX EC+stavudine+nelfinavir
△ ▲ zidovudine/lamivudine+nelfinavir

*This analysis includes all randomized patients through Week 24 and after that point is restricted to patients whose randomization date allows for 36 or 48 weeks of follow-up. The number of patients at each point is indicated below the figure.

Once-Daily VIDEX (didanosine) Buffered Tablet Study

Study AI454-148 was a randomized, open-label, multicenter study comparing treatment with VIDEX Chewable/Dispersible Buffered Tablets (400 mg once daily) plus stavudine (40 mg twice daily) and nelfinavir (750 mg three times daily) versus zidovudine (300 mg twice daily) plus lamivudine (150 mg twice daily) and nelfinavir (750 mg three times daily) in 756 treatment-naive patients, with a mean CD4 cell count of 368 cells/mm^3 (range 80 to 1568 cells/mm^3) and a mean plasma HIV-1 RNA of 4.69 $\log_{10}$ copies/mL (range 2.6 to 5.9 $\log_{10}$ copies/mL) at baseline. The percentages of patients with HIV RNA <400 and <50 copies/mL and not meeting any criteria for treatment failure through 48 weeks are shown in Figure 2.

Figure 2
Treatment Response Through Week 48*, AI454-148



○ ● VIDEX Chewable/Dispersible Buffered Tablets+stavudine+nelfinavir (n=503)
△ ▲ zidovudine+lamivudine+nelfinavir (n=253)

*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. For the differences between treatment groups at 48 weeks, p<0.05 by Cochran-Mantel-Haenszel test.

CONTRAINDICATION

VIDEX EC (didanosine) is contraindicated in patients with previously demonstrated clinically significant hypersensitivity to any component of the formulation.

WARNINGS

1. Pancreatitis

FATAL AND NONFATAL PANCREATITIS HAVE OCCURRED DURING THERAPY WITH DIDANOSINE USED ALONE OR IN COMBINATION REGIMENS IN BOTH TREATMENT-NAIVE AND TREATMENT-EXPERIENCED PATIENTS, REGARDLESS OF DEGREE OF IMMUNOSUPPRESSION. VIDEX EC SHOULD BE SUSPENDED IN PATIENTS WITH SIGNS OR SYMPTOMS OF PANCREATITIS AND DISCONTINUED IN PATIENTS WITH CONFIRMED PANCREATITIS. PATIENTS TREATED WITH VIDEX EC IN COMBINATION WITH STAVUDINE, WITH OR WITHOUT HYDROXYUREA, MAY BE AT INCREASED RISK FOR PANCREATITIS.

When treatment with life-sustaining drugs known to cause pancreatic toxicity is required, suspension of VIDEX EC therapy is recommended. In patients with risk factors for pancreatitis, VIDEX EC should be used with extreme caution and only if clearly indicated. Patients with advanced HIV infection, especially the elderly, are at increased risk of pancreatitis and should be followed closely. Patients with renal impairment may be at greater risk for pancreatitis if treated without dose adjustment.

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

2. Lactic Acidosis/Severe Hepatomegaly with Steatosis

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. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. 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 **PRECAUTIONS: Pregnancy**). Particular caution should be exercised when administering VIDEX EC to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with VIDEX EC should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

3. Retinal Changes and Optic Neuritis

Retinal changes and optic neuritis have been reported in patients taking didanosine. Periodic retinal examinations should be considered for patients receiving VIDEX EC. (See **ADVERSE REACTIONS**.)

PRECAUTIONS

Frequency of Dosing

VIDEX EC should only be administered once daily. There are no data on the use of VIDEX EC dosed more frequently than once daily.

There are limited data to support the long-term durability of response with a once-daily dosing regimen of didanosine. Therefore, the preferred didanosine dosing regimen is twice daily with a VIDEX buffered formulation. Once-daily dosing with VIDEX EC should be considered only for adult patients whose management requires once-daily administration of didanosine or an alternative didanosine formulation (see **Clinical Studies). Consult the prescribing information for VIDEX (didanosine) buffered formulations and Pediatric Powder for Oral Solution for information on twice-daily dosing.**

VIDEX EC should be taken on an empty stomach.

Peripheral Neuropathy

Peripheral neuropathy, manifested by numbness, tingling, or pain in the hands or feet, has been reported in patients receiving didanosine therapy. Peripheral neuropathy has occurred more frequently in patients with advanced HIV disease, in patients with a history of neuropathy, or in patients being treated with neurotoxic drug therapy, including stavudine (see **ADVERSE REACTIONS**).

General

Patients with Renal Impairment

Patients with renal impairment (creatinine clearance <60 mL/min) may be at greater risk of toxicity from didanosine due to decreased drug clearance (see **CLINICAL PHARMACOLOGY**). A dose reduction is recommended in these patients (see **DOSAGE AND ADMINISTRATION**).

Patients with Hepatic Impairment

It is unknown if hepatic impairment significantly affects didanosine pharmacokinetics. Therefore, these patients should be monitored closely for evidence of didanosine toxicity.

Hyperuricemia
Didanosine has been associated with asymptomatic hyperuricemia; treatment suspension may be necessary if clinical measures aimed at reducing uric acid levels fail.

Information for Patients (See **Patient Information Leaflet.)**
Patients should be informed that a serious toxicity of didanosine, used alone and in combination regimens, is pancreatitis, which may be fatal.

Patients should also be aware that peripheral neuropathy, manifested by numbness, tingling, or pain in hands or feet, may develop during therapy with VIDEX EC (didanosine). Patients should be counseled that peripheral neuropathy occurs with greatest frequency in patients with advanced HIV disease or a history of peripheral neuropathy, and that dose modification and/or discontinuation of VIDEX EC may be required if toxicity develops.

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

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

Patients should be informed that the preferred didanosine dosing regimen is twice daily with a VIDEX (didanosine) buffered formulation because there are limited data to support the long-term durability of response with a once-daily regimen.

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

Drug Interactions (see also **CLINICAL PHARMACOLOGY: Drug Interactions)**
Drug interactions that have been established based on drug interaction studies are listed with the pharmacokinetic results in **CLINICAL PHARMACOLOGY: Drug Interactions** (Tables 3-5). The clinical recommendations based on the results of these studies are listed in Table 6.

Table 6
Established Drug Interactions Based on Studies with Buffered Formulations of Didanosine and Expected to Occur with VIDEX EC

Coadministration Not Recommended Based on Drug Interaction Studies (*see* **CLINICAL PHARMACOLOGY: Drug Interactions** *for Magnitude of Interaction*)		
Drug	Effect	Clinical Comment
allopurinol	↑didanosine concentration	Coadministration not recommended.
Alteration in Dose or Regimen Recommended Based on Drug Interaction Studies (*see* **CLINICAL PHARMACOLOGY: Drug Interactions** *for Magnitude of Interaction*)		
Drug	Effect	Clinical Comment
ganciclovir	↑didanosine concentration	Appropriate doses for this combination, with respect to efficacy and safety, have not been established.
methadone	↓didanosine concentration	Appropriate doses for this combination, with respect to efficacy and safety, have not been established.

↑indicates increase.
↓indicates decrease.

Coadministration of VIDEX EC with drugs that are known to cause pancreatitis may increase the risk of this toxicity (see **WARNINGS: Pancreatitis).** Predicted drug interactions with VIDEX EC are listed in Table 7.

Table 7
Predicted Drug Interactions with VIDEX EC

Use with Caution, Risk of Adverse Reactions May Be Increased		
Drug Class	Effect	Clinical Comment
Drugs that may cause pancreatic toxicity	↑risk of pancreatitis	Use only with extreme caution.[a]
Neurotoxic drugs	↑risk of neuropathy	Use with caution.[b]

↑indicates increase.
[a]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 EC is recommended (see **WARNINGS: Pancreatitis**).
[b]See **PRECAUTIONS: Peripheral Neuropathy.**

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

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

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

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

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

Fatal lactic acidosis has been reported in pregnant women who received the combination of didanosine and stavudine with other antiretroviral agents. It is unclear if pregnancy augments the risk of lactic acidosis/hepatic steatosis syndrome reported in non-pregnant individuals receiving nucleoside analogues (see **WARNINGS: Lactic Acidosis/ Severe Hepatomegaly with Steatosis)**. **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.** Health care providers caring for HIV-infected pregnant women receiving didanosine should be alert for early diagnosis of lactic acidosis/hepatic steatosis syndrome.

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

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

Pediatric Use
The safety and efficacy of VIDEX EC in pediatric patients have not been established. Please consult the complete prescribing information for VIDEX (didanosine) buffered formulations and Pediatric Powder for Oral Solution for dosage and administration of didanosine to pediatric patients.

Geriatric Use
In an Expanded Access Program using a buffered formulation of didanosine for the treatment of advanced HIV infection, patients aged 65 years and older had a higher frequency of pancreatitis (10%) than younger patients (5%) (see **WARNINGS**). Clinical studies of didanosine, including those for VIDEX EC, did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently than younger subjects. Didanosine is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection. In addition, renal function should be monitored and dosage adjustments should be made accordingly (see **DOSAGE AND ADMINISTRATION: Dose Adjustment**).

ADVERSE REACTIONS
A SERIOUS TOXICITY OF DIDANOSINE IS PANCREATITIS, WHICH MAY BE FATAL (see **WARNINGS**). OTHER IMPORTANT TOXICITIES INCLUDE LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS; RETINAL CHANGES AND OPTIC NEURITIS; AND PERIPHERAL NEUROPATHY (see **WARNINGS** and **PRECAUTIONS**).

When didanosine is used in combination with other agents with similar toxicities, the incidence of these toxicities may be higher than when didanosine is used alone. Thus, patients treated with VIDEX EC in combination with stavudine, with or without hydroxyurea, may be at increased risk for pancreatitis, which may be fatal, and hepatotoxicity (see **WARNINGS). Patients treated with VIDEX EC in combination with stavudine may also be at increased risk for peripheral neuropathy (**see **PRECAUTIONS).**

Studies of VIDEX EC and a buffered didanosine formulation yielded comparable safety profiles for both formulations. Selected clinical adverse events that occurred in clinical studies of didanosine dosed once daily in combination with other antiretroviral agents are provided in Table 8.

Table 8
Selected Clinical Adverse Events from Combination Studies of Didanosine Dosed Once Daily

	Percent of Patients[a]			
	AI454-152[b]		**AI454-148[c]**	
Adverse Events	VIDEX EC + stavudine + nelfinavir n=255	zidovudine/ lamivudine[d] + nelfinavir n=250	VIDEX Buffered Tablet + stavudine + nelfinavir n=482	zidovudine + lamivudine + nelfinavir n=248
Diarrhea	54	56	70	60
Nausea	21	35	28	40
Headache	20	16	21	30
Peripheral Neurologic Symptoms/Neuropathy	20	8	26	6
Vomiting	13	18	12	14
Rash	10	10	13	16
Pancreatitis (see below)	<1	*	1	*

[a] Percentages based on treated patients.
[b] Median duration of treatment 43 weeks in the VIDEX EC+stavudine+nelfinavir group and 39 weeks in the zidovudine/lamivudine+nelfinavir group.
[c] Median duration of treatment 48 weeks.
[d] Zidovudine/lamivudine combination tablet.
* This event was not observed in this study arm.

In clinical trials using a buffered formulation of didanosine, pancreatitis resulting in death was observed in one patient who received didanosine plus stavudine plus nelfinavir, one patient who received didanosine plus stavudine plus indinavir, and 2 of 68 patients who received didanosine plus stavudine plus indinavir plus hydroxyurea. In an early access program, pancreatitis resulting in death was observed in one patient who received VIDEX EC plus stavudine plus hydroxyurea plus ritonavir plus indinavir plus efavirenz (see **WARNINGS).**

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

Selected laboratory abnormalities that occurred in clinical studies of didanosine dosed once daily in combination with other antiretroviral agents are shown in Table 9.

Table 9
Selected Laboratory Abnormalities from Combination Studies of Didanosine Dosed Once Daily

	Percent of Patients[a]							
	AI454-152[b]				**AI454-148[c]**			
	VIDEX EC + stavudine + nelfinavir n=255		zidovudine/ lamivudine[d] +nelfinavir n=250		VIDEX Buffered Tablet+ stavudine+ nelfinavir n=482		zidovudine + lamivudine + nelfinavir n=248	
Parameter	Grades 3-4[e]	All Grades	Grades 3-4[e]	All Grades	Grades 3-4[e]	All Grades	Grades 3-4[e]	All Grades
SGOT (AST)	4	40	4	17	3	42	2	23
SGPT (ALT)	4	39	4	20	3	37	3	24
Lipase	3	18	<1	8	7	17	2	11
Bilirubin	<1	7	<1	3	<1	7	<1	3

[a] Percentages based on treated patients.
[b] Median duration of treatment 43 weeks in the VIDEX EC+stavudine+nelfinavir group and 39 weeks in the zidovudine/lamivudine+nelfinavir group.
[c] Median duration of treatment 48 weeks.
[d] Zidovudine/lamivudine combination tablet.
[e] >5 x ULN for SGOT and SGPT, ≥2.1 x ULN for lipase, and ≥2.6 x ULN for bilirubin (ULN = upper limit of normal).

Observed during Clinical Practice
The following events have been identified during postapproval use of didanosine buffered formulations. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to their seriousness, frequency of reporting, causal connection to didanosine, or a combination of these factors.

Body as a Whole – abdominal pain, alopecia, anaphylactoid reaction, asthenia, chills/fever, and pain.
Digestive Disorders – anorexia, dyspepsia, and flatulence.
Exocrine Gland Disorders – pancreatitis (including fatal cases) (see **WARNINGS**), sialoadenitis, parotid gland enlargement, dry mouth, and dry eyes.
Hematologic Disorders – anemia, leukopenia, and thrombocytopenia.
Liver – lactic acidosis and hepatic steatosis (see **WARNINGS**); hepatitis and liver failure.
Metabolic Disorders - diabetes mellitus, elevated serum alkaline phosphatase level, elevated serum amylase level, elevated serum gamma-glutamyltransferase level, elevated serum uric acid level, hypoglycemia, and hyperglycemia.
Musculoskeletal Disorders - myalgia (with or without increases in creatine kinase), rhabdomyolysis including acute renal failure and hemodialysis, arthralgia, and myopathy.
Ophthalmologic Disorders - retinal depigmentation and optic neuritis (see **WARNINGS**).

OVERDOSAGE
There is no known antidote for didanosine overdosage. In phase 1 studies, in which buffered formulations of didanosine were initially administered at doses ten times the currently recommended dose, toxicities included: pancreatitis, peripheral neuropathy, diarrhea, hyperuricemia, and hepatic dysfunction. Didanosine is not dialyzable by peritoneal dialysis, although there is some clearance by hemodialysis (see **CLINICAL PHARMACOLOGY: Pharmacokinetics**).

DOSAGE AND ADMINISTRATION

Dosage

Adults

VIDEX EC (didanosine) should be administered on an empty stomach.

VIDEX EC Delayed-Release Capsules should be swallowed intact.

The recommended daily dose is dependent on body weight and is administered as one capsule given on a once-daily schedule as outlined in Table 10.

Table 10
Dosing of VIDEX EC Delayed-Release Capsules

Patient Weight	Dosage
≥60 kg	400 mg once daily
<60 kg	250 mg once daily

Pediatric Patients

VIDEX EC has not been studied in pediatric patients. Please consult the complete prescribing information for VIDEX (didanosine) buffered formulations and Pediatric Powder for Oral Solution for dosage and administration of didanosine to pediatric patients.

Dose Adjustment

Clinical and laboratory signs suggestive of pancreatitis should prompt dose suspension and careful evaluation of the possibility of pancreatitis. VIDEX EC use should be discontinued in patients with confirmed pancreatitis (see **WARNINGS).**

Based on data with buffered didanosine formulations, patients with symptoms of peripheral neuropathy may tolerate a reduced dose of VIDEX EC after resolution of the symptoms of peripheral neuropathy upon drug interruption. If neuropathy recurs after resumption of VIDEX EC, permanent discontinuation of VIDEX EC should be considered.

Renal Impairment

Dosing recommendations for VIDEX EC and VIDEX buffered formulations are different for patients with renal impairment. Please consult the complete prescribing information on administration of VIDEX (didanosine) buffered formulations to patients with renal impairment.

In adult patients with impaired renal function, the dose of VIDEX EC should be adjusted to compensate for the slower rate of elimination. The recommended doses and dosing intervals of VIDEX EC in adult patients with renal insufficiency are presented in Table 11.

Table 11
Recommended Dosage of VIDEX EC in Renal Impairment by Body Weight[a]

Creatinine Clearance (mL/min)	Dosage	
	≥60 kg	<60 kg
≥60	400 once daily	250 once daily
30-59	200 once daily	125 once daily
10-29	125 once daily	125 once daily
<10	125 once daily	b

[a] Based on studies using a buffered formulation of didanosine.
[b] Not suitable for use in patients <60 kg with CL_{cr} <10 mL/min. An alternate formulation of didanosine should be used.

Patients Requiring Continuous Ambulatory Peritoneal Dialysis (CAPD) or Hemodialysis

For patients requiring CAPD or hemodialysis, follow dosing recommendations for patients with creatinine clearance less than 10 mL/min, shown in Table 11. It is not necessary to administer a supplemental dose of didanosine following hemodialysis.

Hepatic Impairment (See **WARNINGS** and **PRECAUTIONS**.)

HOW SUPPLIED

VIDEX® EC (didanosine) Delayed-Release Capsules are white, opaque capsules that are packaged in bottles with child-resistant closures as described in Table 12.

Table 12
VIDEX EC Delayed-Release Capsules

125 mg capsule imprinted with BMS 125 mg 6671 in Tan	
NDC No. 0087-6671-17	30 capsules/bottle
NDC No. 0087-6671-12	60 capsules/bottle
200 mg capsule imprinted with BMS 200 mg 6672 in Green	
NDC No. 0087-6672-17	30 capsules/bottle
NDC No. 0087-6672-12	60 capsules/bottle
250 mg capsule imprinted with BMS 250 mg 6673 in Blue	
NDC No. 0087-6673-17	30 capsules/bottle
NDC No. 0087-6673-12	60 capsules/bottle
400 mg capsule imprinted with BMS 400 mg 6674 in Red	
NDC No. 0087-6674-17	30 capsules/bottle
NDC No. 0087-6674-12	60 capsules/bottle

The capsules should be stored in tightly closed containers at 25° C (77° F). Excursions between 15° and 30° C (59° and 86° F) are permitted [see USP Controlled Room Temperature].

HANDLING AND DISPOSAL

Disposal options include incineration, landfill, or sewer as dictated by specific circumstances and relevant national, state, and local regulations.

US Patent Nos: 4,861,759 and 5,616,566 (didanosine).
Patent also Pending (didanosine capsules).

BRISTOL-MYERS SQUIBB
IMMUNOLOGY

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Princeton, NJ 08543 USA

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Patient Information

Rx only

VIDEX® EC

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

VIDEX® EC (didanosine) Delayed-Release Capsules
Enteric-Coated Beadlets

What is VIDEX EC?

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

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

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

There is limited information on the antiviral response of long-term use of VIDEX EC.

In VIDEX EC, an enteric coating is used to protect the medicine while it is in your stomach since stomach acids can break it down. The enteric coating dissolves when the medicine reaches your small intestine.

Who should not take VIDEX EC?

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

Because it has only been studied in adults, VIDEX EC is not recommended for children.

How should I take VIDEX EC?
How should I store it?

VIDEX EC should only be taken once daily. VIDEX EC has been prescribed for you because your doctor believes that a once-daily dosing schedule of didanosine (the active ingredient in VIDEX EC) is right for you. The preferred dosing schedule of didanosine is twice daily with the VIDEX tablet or liquid form.

Your doctor will determine your dose based on your body weight, kidney and liver function, and any side effects that you may have had with other medicines. Take VIDEX EC **on an empty stomach. Do not take VIDEX EC with food.** Swallow the capsule whole; do not open it. Try not to miss a dose, but if you do, take it as soon as possible. If it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule.

Store capsules in a tightly closed container at room temperature away from heat and out of the reach of children and pets.

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

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

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

What should I avoid while taking VIDEX EC?

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

Other medicines. Other medicines, including those you can buy without a prescription, may interfere with the actions of VIDEX EC. **Do not take any medicine, vitamin supplement, or other health preparation without first checking with your doctor.**

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

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

What are the possible side effects of VIDEX EC?

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

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

- feeling very weak, tired, or uncomfortable,
- unusual or unexpected stomach discomfort,
- feeling cold,
- feeling dizzy or lightheaded,
- suddenly developing a slow or irregular heartbeat.

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

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

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

Peripheral neuropathy. This is a problem with the nerves in your hands or feet. The nerve problem may be serious. ***Tell your doctor right away if you have continuing numbness, tingling, or pain in the feet or hands.***

Before starting VIDEX EC therapy, let your doctor know if you have ever had peripheral neuropathy. This condition is more likely to happen in people who have had it before. It is also more likely in patients taking medicines that affect the nerves and in people with advanced HIV disease. However, it can occur at any stage of HIV disease. If you get peripheral neuropathy, your doctor will tell you to stop taking VIDEX EC. After stopping VIDEX EC, the symptoms may get worse for a short time and then get better. Once symptoms of peripheral neuropathy go away completely, you and your doctor should decide if starting VIDEX EC is right for you. If so, you might be started at a lower dose.

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

Other side effects: The most common side effects in adults taking VIDEX EC in combination with other HIV drugs included diarrhea, nausea, headache, vomiting, and rash.

Inactive Ingredients:
Carboxymethylcellulose sodium 12, diethyl phthalate, methacrylic acid copolymer, sodium hydroxide, sodium starch glycolate, talc, colloidal silicon dioxide, gelatin, sodium lauryl sulfate, and titanium dioxide.

This medicine was prescribed for your particular condition. Do not use VIDEX EC for another condition or give it to others. Keep VIDEX EC and all medicines out of the reach of children. Throw away VIDEX EC when it is outdated or no longer needed by flushing it down the toilet or pouring it down the sink.

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

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

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