Bristol-Myers Squibb

January 2006

RE: Discontinuation of Sale and Distribution of VIDEX® (didanosine) Chewable/Dispersible Buffered Tablets

Dear Health Care Professional:

Bristol-Myers Squibb would like to inform you that the sale and distribution of all strengths of VIDEX® (didanosine) Chewable/Dispersible Buffered Tablets in the United States will be discontinued effective immediately. This action is voluntary and is not the result of any safety or efficacy issues regarding the product.

Table 1. VIDEX Chewable/Dispersible Buffered Tablets Being Discontinued Effective Immediately

NDC No.	Packaging Information	Product Strength
0087-6650-01	60 tablets/bottle	25 mg/tablet
0087-6651-01	60 tablets/bottle	50 mg/tablet
0087-6652-01	60 tablets/bottle	100 mg/tablet
0087-6653-01	60 tablets/bottle	150 mg/tablet
0087-6665-15	60 tablets/bottle	200 mg/tablet

Table 2. Currently Available Formulations of VIDEX Pediatric Powder for Oral Solution and VIDEX EC Delayed-Release Capsules

Videx Pediatric Powder for Oral Solution		
NDC No.	**Packaging Information**	**Product Strength**
0087-6632-41	One bottle per carton	2 g/bottle
0087-6633-41	One bottle per carton	4 g/bottle
Videx EC Delayed-Release Capsules		
NDC No.	**Packaging Information**	**Product Strength**
0087-6671-17	30 capsules/bottle	125 mg/capsule
0087-6672-17	30 capsules/bottle	200 mg/capsule
0087-6673-17	30 capsules/bottle	250 mg/capsule
0087-6674-17	30 capsules/bottle	400 mg/capsule

Options for continuing didanosine therapy in patients who are currently receiving VIDEX Chewable/Dispersible Buffered Tablets are to change therapy to VIDEX® EC (didanosine) Delayed-Release Capsules Enteric-Coated Beadlets or to utilize VIDEX Pediatric Powder for Oral Solution.

Some considerations when changing therapy from VIDEX Chewable/Dispersible Buffered Tablets to VIDEX EC capsules include the following:

- The bioavailability of didanosine from the VIDEX tablets is equivalent to that of VIDEX EC capsules. If the patient would normally receive a 200 mg dose of VIDEX tablets twice daily, then the dose of VIDEX EC would be one 400 mg capsule once daily.
- VIDEX EC capsules are swallowed whole and should not be opened, while VIDEX buffered tablets need to be chewed or dispersed in water.

- VIDEX EC can only be administered as one capsule once a day, while, to provide adequate buffering, the adult dosing of VIDEX buffered tablets is at least two of the appropriate strength tablets, but no more than four tablets to be thoroughly chewed or dispersed in at least 1 ounce of water prior to consumption.
- VIDEX EC (didanosine) contains no buffer. Buffer may cause stomach upset in some patients, and be associated with a bitter and chalky taste. Because there is no buffer in VIDEX EC, some buffer-related drug interactions seen with the VIDEX (didanosine) tablet formulations are eliminated.
- All VIDEX formulations, including VIDEX EC, should be administered on an empty stomach.
- To avoid the possibility of an overdose with didanosine, patients should be counseled that changing to VIDEX EC capsules from VIDEX tablets will result in a lower daily pill count for didanosine.

Some considerations when changing therapy from VIDEX Chewable/Dispersible Buffered Tablets to VIDEX Pediatric Powder for Oral Solution include the following:

- Adults can use VIDEX Pediatric Powder for Oral Solution.
- The bioavailability of didanosine from the VIDEX Pediatric Powder for Oral Solution is equivalent to that of the tablet. If the patient would normally receive a 200 mg dose of VIDEX tablets twice daily, then the dose of VIDEX Pediatric Powder for Oral Solution would also be 200 mg twice daily.
- Adequate gastric buffering is necessary for administration of the Pediatric Powder. Instructions for the preparation of the oral solution are provided below.

Preparation of VIDEX Pediatric Powder for Oral Solution

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

20 mg/mL Initial Solution – Constitute the product to 20 mg/mL by adding 100 mL or 200 mL of Purified Water, USP, to the 2 g or 4 g of VIDEX powder, respectively, in the product bottle.

10 mg/mL Final Admixture – 1. Immediately mix one part of the 20 mg/mL initial solution with one part of Maximum Strength Mylanta® Liquid for a final dispensing concentration of 10 mg VIDEX per mL. For patient home use, the admixture should be dispensed in appropriately sized, flint-glass or plastic (HDPE, PET, or PETG) bottles with child-resistant closures. This admixture is stable for 30 days under refrigeration, 36º to 46º F (2º to 8º C).

2. Instruct the patient to shake the admixture thoroughly prior to use and to store the tightly closed container in the refrigerator, 36º to 46º F (2º to 8º C), up to 30 days.

Important information about VIDEX and VIDEX EC

VIDEX® (didanosine) Chewable/Dispersible Buffered Tablets
VIDEX® (didanosine) Pediatric Powder for Oral Solution

INDICATION:
VIDEX (didanosine) in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection.

IMPORTANT SAFETY INFORMATION:

- **Fatal and non-fatal pancreatitis have occurred during therapy with VIDEX (didanosine) used alone or in combination regimens in both treatment-naïve 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.**

- **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.**

- Retinal changes and optic neuritis have been reported in patients taking VIDEX.

- The safety and efficacy of VIDEX have not been established in HIV-infected patients with significant underlying liver disease. If there is evidence of worsening liver disease in patients with preexisting liver dysfunction, interruption or discontinuation of treatment must be considered.

- Peripheral neuropathy, manifested by numbness, tingling, or pain in the hands or feet, has been reported in patients receiving didanosine therapy.

- Redistribution and/or accumulation of body fat have been seen in patients receiving antiretroviral therapy. A causal relationship has not been established.

- Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including VIDEX.

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

- Coadministration of VIDEX with drugs that are known to cause pancreatitis may increase the risk of this toxicity.

- Coadministration of tenofovir disoproxil fumarate with VIDEX should be undertaken with caution, and patients should be monitored closely for didanosine-related toxicities, including pancreatitis, symptomatic hyperlactatemia/lactic acidosis, and peripheral neuropathy and clinical response. VIDEX should be suspended if signs or symptoms of pancreatitis, symptomatic hyperlactatemia, or lactic acidosis develop.

- Coadministration of didanosine and allopurinol or ribavirin is not recommended. Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis have been reported in patients receiving both VIDEX and ribavirin.

- The risk for pancreatitis, hepatotoxicity and peripheral neuropathy which was severe in some cases, may be increased for patients treated with VIDEX in combination with stavudine, with or without hydroxyurea.

- Frequent side effects reported in VIDEX (didanosine)-containing triple combination regimens are diarrhea (70%), nausea (53%), headache (46%), rash (30%), vomiting (30%), and peripheral neurologic symptoms/neuropathy (26%).

- All VIDEX formulations should be administered on an empty stomach at least 30 minutes before or two hours after eating.

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

INDICATION:
VIDEX EC (didanosine) in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection in adults.

IMPORTANT SAFETY INFORMATION:

- **Fatal and non-fatal pancreatitis have occurred during therapy with didanosine used alone or in combination regimens in both treatment-naïve 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.**

- **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.**

- Retinal changes and optic neuritis have been reported in patients taking VIDEX EC.

- The safety and efficacy of VIDEX EC have not been established in HIV-infected patients with significant underlying liver disease. If there is evidence of worsening liver disease in patients with preexisting liver dysfunction, interruption or discontinuation of treatment must be considered.

- Peripheral neuropathy, manifested by numbness, tingling, or pain in the hands or feet, has been reported in patients receiving didanosine therapy.

- Redistribution and/or accumulation of body fat have been seen in patients receiving antiretroviral therapy. A causal relationship has not been established.

- Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including VIDEX EC.

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

- Coadministration of VIDEX EC with drugs that are known to cause pancreatitis may increase the risk of this toxicity.

- Coadministration of tenofovir disoproxil fumarate with VIDEX EC (didanosine) should be undertaken with caution, and patients should be monitored closely for didanosine-related toxicities, including pancreatitis, symptomatic hyperlactatemia/lactic acidosis, and peripheral neuropathy, and clinical response. VIDEX EC should be suspended if signs or symptoms of pancreatitis, symptomatic hyperlactatemia, or lactic acidosis develop.

- Coadministration of didanosine and allopurinol or ribavirin is not recommended. Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis have been reported in patients receiving both VIDEX EC and ribavirin.

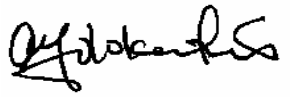
- The risk for pancreatitis, hepatotoxicity and peripheral neuropathy which was severe in some cases, may be increased for patients treated with VIDEX EC in combination with stavudine, with or without hydroxyurea.

- Frequent side effects reported in VIDEX EC-containing triple combination regimens are diarrhea (57%), peripheral neurologic symptoms/neuropathy (25%), nausea (24%), headache (22%), rash (14%), and vomiting (14%).

- VIDEX EC should be administered once daily on an empty stomach and swallowed intact.

Please see the enclosed Full Prescribing Information for VIDEX (didanosine) and VIDEX EC (didanosine). If you have questions or require additional information regarding the discontinuation of VIDEX Chewable/Dispersible Buffered Tablets, please contact our Medical Information Department at 1-800-321-1335.

Sincerely,



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Encl: VIDEX and VIDEX EC Package Inserts

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