

Didanosine

Brand Name: Videx, Videx EC

Drug Class: Nucleoside Reverse Transcriptase Inhibitors

Drug Description

Didanosine, a synthetic antiretroviral agent, is a nucleoside reverse transcriptase inhibitor. [1] Didanosine, a synthetic antiretroviral agent, is a synthetic analogue of deoxyadenosine, a naturally occurring purine nucleoside. Didanosine differs from deoxyadenosine in that the 3'-hydroxyl group on the ribose moiety is replaced with hydrogen. [2]

HIV/AIDS-Related Uses

Didanosine was approved by the FDA on October 9, 1991, and enteric-coated didanosine was approved by the FDA on October 31, 2000.[3] A generic delayed-release capsule formulation was approved by the FDA on December 3, 2004.[4] Didanosine is used in conjunction with other antiretroviral agents for the treatment of HIV-1 infection in adults, adolescents, and pediatric patients.[5]

Didanosine is used with other antiretrovirals for postexposure prophylaxis of HIV infection in health care workers and other individuals exposed occupationally via percutaneous injury or mucous membrane or nonintact skin contact with tissues or body fluids associated with a risk of HIV transmission.[6]

Because of a decline in clinical demand for the buffered tablet formulation of didanosine, this formulation was discontinued in the U.S. by the manufacturer in February 2006. The discontinuation of the less popular buffered tablets is voluntary and does not reflect any problems with safety or efficacy.[7]

Pharmacology

Didanosine is converted by cellular enzymes to the active metabolite 2,3-dideoxyadenosine-5-triphosphate (ddA-TP), which inhibits HIV-1 reverse transcriptase by competing with the natural substrate, deoxyadenosine 5'-triphosphate, for incorporation into viral DNA. Once incorporated, ddA-TP causes termination of viral DNA synthesis.[8]

Didanosine is acid labile. All oral formulations of didanosine contain or are compounded with buffering agents to increase gastric pH.[9] Didanosine is rapidly absorbed, with peak plasma concentrations (C_{max}) observed from 0.25 to 1.50 hours following oral dosing with a buffered formulation (in tablet or powder form) and 2 hours following oral dosing with the enteric-coated formulation. Extent of absorption depends on several factors, including dosage form, gastric pH, and presence of food in the gastrointestinal (GI) tract. There is considerable variation between individuals in C_{max} and areas under the plasma concentration curve (AUC) of didanosine attained following oral administration.[10]

Didanosine's C_{max} and AUC were decreased by approximately 55% when didanosine buffered tablets were administered up to 2 hours after a meal. Administration of didanosine tablets up to 30 minutes before a meal did not result in any significant changes in bioavailability. The C_{max} and AUC for the enteric-coated formulation were reduced by approximately 46% and 19%, respectively, in the presence of food.[11]

Because gastric secretions may inactivate didanosine following oral administration, didanosine chewable/dispersible tablets and powder for oral solution either contain buffering agents or must be admixed with antacids prior to administration. Each adult dose of the buffered tablet formulation of didanosine must consist of 2 tablets to ensure adequate acid-neutralizing capacity.[12] The delayed-release capsules contain enteric-coated beadlets, which protect didanosine from degradation by stomach acid.[13]

Didanosine is distributed into cerebrospinal fluid (CSF) following IV administration. CSF concentrations average 19% to 21% of concurrent plasma concentrations in samples obtained 1 hour after a single IV dose. In a study of HIV infected pediatric patients who received oral or intravenous didanosine, CSF concentrations averaged 46% (over a range of 12% to 85%) of concurrent plasma concentrations.[14] Binding of didanosine to plasma proteins in vitro is less than 5%.[15]

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Pharmacology (cont.)

Didanosine is in FDA Pregnancy Category B. No adequate or well-controlled studies of didanosine have been done in pregnant women. In animal studies, didanosine and/or its metabolites were transferred to the fetus through the placenta. Animal studies with didanosine have not shown evidence of impaired fertility or harm to the fetus. Nevertheless, the drug should be used during pregnancy only if clearly needed. To monitor maternal-fetal outcomes of pregnant women exposed to didanosine and other antiretroviral agents, an Antiretroviral Pregnancy Registry has been established. Physicians may register patients online at <http://www.APRegistry.com> or by calling 1-800-258-4263.[16] It is not known whether didanosine or its metabolites are distributed into human milk; however, the drug and/or its metabolites are distributed into milk in laboratory animals. Because of both the potential for HIV transmission and serious adverse reactions in nursing infants, HIV infected mothers should be instructed not to breastfeed their infants if they are receiving didanosine.[17]

The metabolic fate of didanosine has not been fully evaluated in humans. Because didanosine is an analogue of a naturally occurring purine nucleoside, metabolism of the drug is presumed to occur via the same pathways as endogenous purines. The in vivo intracellular half-life of the active metabolite, ddA-TP, has not been determined; the in vitro intracellular half-life of ddA-TP is 8 to 24 hours. In HIV infected adults, the plasma half-life of didanosine averages 0.97 to 1.6 hours. In HIV infected pediatric patients, the plasma half-life averages 0.8 hours.[18]

Didanosine is eliminated in urine by glomerular filtration and active tubular secretion. Following oral dosing in adults, the renal clearance of didanosine is approximately 50% of the total body clearance and averages 400 ml/min. Renal clearance has been reported to average 5.5 ml/min/kg in adult patients and 240 ml/min/m² in pediatric patients. In HIV infected adults, approximately 20% of the dose is eliminated in the urine; in pediatric patients approximately 18% of the dose is eliminated in the urine.[19]

The half-life of didanosine increases as creatinine clearance decreases. It is recommended that the didanosine dose be modified in patients with renal impairment and reduced creatinine clearance and in patients receiving maintenance hemodialysis.[20] A 4-hour hemodialysis session reduces the serum didanosine concentration by approximately 20%.[21] The effects of impaired hepatic function on the pharmacokinetics of didanosine have not been adequately studied.[22]

HIV-1 isolates with reduced sensitivity to didanosine have been selected in vitro and were also obtained from patients treated with didanosine. Phenotypic analysis of HIV-1 isolates from 60 patients receiving from 6 to 24 months of didanosine monotherapy, some with prior exposure to zidovudine, 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.[23]

HIV-1 isolates from 2 of 39 patients receiving combination therapy with zidovudine and didanosine for up to 2 years exhibited cross-resistance to zidovudine, didanosine, zalcitabine, stavudine, and lamivudine in vitro. The clinical relevance of these observations has not been established.[24]

Further study is needed to evaluate more fully the extent of cross resistance among the dideoxynucleoside reverse transcriptase inhibitors. Although zidovudine-resistant HIV strains are susceptible to didanosine in vitro, some zidovudine-resistant strains may be cross resistant to didanosine or zalcitabine. In addition, some strains of HIV modified in vitro by site-directed mutagenesis have had decreased susceptibility to both didanosine and zalcitabine but were susceptible to zidovudine.[25]

Cross resistance between didanosine and protein inhibitors (PIs), including amprenavir, indinavir, lopinavir, nelfinavir, ritonavir, and saquinavir, is highly unlikely since the drugs have different target enzymes. The potential for cross resistance between didanosine and non-nucleoside reverse transcriptase inhibitors (delavirdine, efavirenz, and nevirapine) is considered to be low since the drugs bind on different sites of reverse transcriptase and have

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Pharmacology (cont.)

different mechanisms of action.[26]

Adverse Events/Toxicity

Fatal and nonfatal pancreatitis has occurred during therapy with didanosine used alone or in combination regimens in both treatment-naive and treatment-experienced patients, regardless of degree of immunosuppression. Didanosine should be suspended in patients with signs or symptoms of pancreatitis and discontinued in patients with confirmed pancreatitis. Patients treated with didanosine 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 didanosine therapy is recommended. In patients with risk factors for pancreatitis, didanosine 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, as indicated in Phase III trials using buffered formulations of didanosine, with an incidence in adult patients of 1% to 10% in doses higher than currently recommended and 1% to 7% with recommended doses.[27]

The use of didanosine and other nucleoside analogues, either alone or in combination with other antiretrovirals, has been associated with lactic acidosis and severe hepatomegaly with steatosis, including some fatal cases. Risk factors include female gender, obesity, and prolonged exposure to antiretroviral nucleoside analogues. Fatal lactic acidosis has been reported in pregnant women who received an antiretroviral regimen that included didanosine and stavudine. Cases have occurred in patients with and without known risk factors for liver disease. Didanosine use 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.[28]

Retinal changes and optical neuritis have been reported in patients taking didanosine. Periodic retinal examinations should be considered for patients taking didanosine.[29]

Peripheral neuropathy, manifested by numbness, tingling, or pain in the hands or feet, has been reported in patients taking didanosine. Redistribution or accumulation of body fat, including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance," have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown. A causal relationship has not been established.[30]

Common, less serious adverse effects include central nervous system effects (anxiety, headache, insomnia, irritability, and restlessness), dry mouth, GI disturbances (diarrhea, dyspepsia, flatulence, nausea, vomiting), and skin rash.[31]

Drug and Food Interactions

Presence of food in the GI tract decreases the rate and extent of absorption of oral didanosine. Antacids increase the oral bioavailability of didanosine.[32]

The manufacturer suggests that didanosine be discontinued in patients who require life-sustaining treatment with other drugs known to cause pancreatitis. Patients receiving didanosine in combination with stavudine, with or without hydroxyurea, may be at an increased risk for potentially fatal pancreatitis.[33]

Didanosine and some (PIs), including amprenavir, indinavir, nelfinavir, ritonavir, and saquinavir, have additive or synergistic activity against HIV-1, probably due to the different stages of virus replication at which these drugs are active. However, due to the buffering agents in some didanosine dosage forms and the requirement that most PIs be administered with food, dosing of these drugs should be separated.[34]

Concomitant use of allopurinol and didanosine is not recommended. Allopurinol may increase

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Drug and Food Interactions (cont.)

plasma AUC of didanosine by two- to fourfold. In clinical studies, AUC and Cmax of didanosine increased 113% and 69%, respectively, when administered concomitantly with allopurinol in healthy adults.[35]

Concomitant use of didanosine and drugs associated with pancreatic toxicity, such as alcohol, asparaginase, azathioprine, estrogens, furosemide, methyl dopa, nitrofurantoin, pentamidine (IV), sulfonamides, sulindac, tetracyclines, thiazide diuretics, and valproic acid, may increase the risk of pancreatitis. Didanosine should be used with extreme caution and only when other alternatives are not available in patients receiving these drugs.[36]

Didanosine should be avoided or used with caution in patients receiving other drugs that have been associated with peripheral neuropathy, such as chloramphenicol, cisplatin, dapsone, ethambutol, ethionamide, hydralazine, isoniazid, lithium, metronidazole, nitrofurantoin, nitrous oxide, phenytoin, stavudine, vincristine, and zalcitabine.[37]

When buffered preparations of didanosine are administered with medications that require an acidic environment, didanosine may cause decreased absorption of the coadministered drug. Drugs that depend on gastric acidity for optimal absorption, including dapsone, itraconazole, and ketoconazole, should be administered at least 2 hours before or 2 hours after didanosine is given.[38]

Concurrent administration of delavirdine or indinavir and didanosine may decrease absorption of these drugs. If either of these drugs are taken together, delavirdine or indinavir should be given 1 hour prior to didanosine administration.[39]

Coadministration of tenofovir disoproxil fumarate (tenofovir DF) with didanosine causes increased absorption of didanosine. Increased exposure may cause or worsen didanosine-related toxicities, including pancreatitis, hyperlactatemia/lactic acidosis, and peripheral neuropathy. Coadministration of tenofovir DF with didanosine should be undertaken with caution, and patients

should be monitored closely for didanosine-related toxicities.[40]

In vitro studies demonstrate that concurrent administration of didanosine and oral ganciclovir resulted in a 111% increase in the steady-state AUC of didanosine and may result in increased didanosine-related toxicities. Because valganciclovir is rapidly and completely converted to ganciclovir, drug interactions associated with ganciclovir are expected to occur with valganciclovir as well. Patients receiving concomitant therapy with didanosine and ganciclovir or valganciclovir should be monitored for didanosine toxicity.[41]

The oral absorption and plasma concentrations of fluoroquinolone antibiotics or tetracyclines may be decreased in the presence of antacids such as those present in the buffering agents of certain oral didanosine dosage forms. Dosages of didanosine and quinolones should be separated by at least 2 hours.[42]

Exposure to didanosine or its active metabolite (dideoxyadenosine 5'-triphosphate) is increased when didanosine is coadministered with ribavirin. Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and hyperlactatemia/lactic acidosis have been reported in patients taking both didanosine and ribavirin. Coadministration of ribavirin with didanosine is not recommended.[43]

Based on data from an open-label randomized study and retrospective database analyses, clinicians are advised to use caution when administering enteric-coated didanosine, tenofovir DF, and either efavirenz or nevirapine in the treatment of treatment-naïve HIV infected patients with high baseline viral loads.[44]

Contraindications

Didanosine is contraindicated in patients with previously demonstrated, clinically significant hypersensitivity to any component of the formulation.[45]

Risk-benefit should be considered in patients with peripheral neuropathy; active alcoholism; history of or current hypertriglyceridemia; history of

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Contraindications (cont.)

pancreatitis; or conditions requiring a low-sodium diet, including cardiac failure, cirrhosis of the liver, severe hepatic disease, peripheral or pulmonary edema, hypernatremia, hypertension, renal function impairment, toxemia of pregnancy, gouty arthritis, hepatic function impairment, or phenylketonuria.[46]

Patients with phenylketonuria should be made aware that didanosine chewable buffered tablets contain up to 73 mg of phenylalanine per two-tablet dose.[47]

Clinical Trials

For information on clinical trials that involve Didanosine, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Didanosine AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[48]

Dosage Form: Chewable buffered tablets containing didanosine 25, 50, 100, 150, or 200 mg.[49]

Buffered powder for oral solution in single-dose packets containing didanosine 100, 167, or 250 mg.[50]

Pediatric powder for oral solution in 4- or 8-ounce bottles containing didanosine 2 or 4 g, respectively.[51]

Delayed-release capsules of enteric-coated beadlets containing didanosine 125, 200, 250, or 400 mg.[52]

Bioequivalent generic delayed-release capsules containing didanosine 200, 250, or 400 mg.[53]

The recommended dose of didanosine in pediatric patients who weigh at least 20 kg and who can swallow capsules is based on body weight according to the following scale: Patients who weigh 20 to <25 kg should receive didanosine 200 mg once daily; 25 to <60 kg, 250 mg once daily;

and 60 kg or more, 400 mg once daily.[54] For patients who weigh less than 20 kg, the recommended dose of didanosine powder for oral solution is based on age and body surface area: pediatric patients aged 2 weeks to 8 months should receive 100 mg/m² twice daily, and pediatric patients older than 8 months should receive 120 mg/m² twice daily.[55]

In patients with impaired renal function, the doses and dosing intervals of didanosine should be adjusted to compensate for the slower rate of elimination. Recommendations for didanosine dosing in renal impairment are provided in the Videx and Videx EC prescribing information from the manufacturer.[56] In patients who have hepatic impairment, no dosage adjustment is necessary. Similar ranges of maximum plasma concentrations and areas under the concentration-time curve were observed in a study of participants who had impairment and those who were matched controls.[57]

Storage: Store didanosine chewable/dispersible tablets and powder for oral solution between 15 C and 30 C (59 F and 86 F). Delayed-release capsules should be stored at 25 C (77 F), with excursions between 15 C and 30 C (59 F and 86 F) permitted.[58]

Chemistry

CAS Name: Inosine, 2',3'-dideoxy-[59]

CAS Number: 69655-05-6[60]

Molecular formula: C₁₀H₁₂N₄O₃[61]

C50.84%, H5.12%, N23.72%, O20.32%[62]

Molecular weight: 236.23[63]

Melting point: 160 to 163 C[64]

Physical Description: White crystalline powder.[65]

Stability: Didanosine is stable at neutral or slightly alkaline pH, but is unstable at acid pH.[66] To provide adequate buffering, at least two of the appropriate strength tablets of the buffered

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Chemistry (cont.)

formulation (but no more than 4 tablets) should be thoroughly chewed or dispersed in at least 1 ounce of water prior to consumption. Solutions made from didanosine chewable/dispersible buffered tablets that have been dispersed in water or dispersed in clear apple juice are stable for 1 hour at room temperature. The dispersion should be stirred just prior to consumption.[67]

After reconstitution with the appropriate admixture of water and liquid antacid by a pharmacist, the resulting suspension of didanosine pediatric powder for oral solution may be stored for up to 30 days in a refrigerator at 2 C to 8 C (36 F to 46 F). Discard any unused portion after 30 days.[68]

Solubility: 27.3 mg/ml in aqueous solution of pH 6 at 25 C.[69]

Other Names

BMY 40900[70]

CCRIS 805[71]

ddI[72]

Dideoxyinosine[73]

BRN 3619529[74]

HSDB 6548[75]

Further Reading

Cooper DA. Update on didanosine. *J Int Assoc Physicians AIDS Care (Chic Ill)*. 2002 Winter; 1(1): 15-2Crespo M, Ribera E, Suárez-Lozano I, Domingo P, Pedrol E, López-Aldeguer J, Muñoz A, Viladés C, Sánchez T, Viciano P, Teira R, García-Alcalde ML, Vergara A, Lozano F, Galindo MJ, Cosin J, Roca B, Terrón A, Geijo P, Vidal F, Garrido M; VACH Cohort Study Group. Effectiveness and safety of didanosine, lamivudine and efavirenz versus zidovudine, lamivudine and efavirenz for the initial treatment of HIV-infected patients from the Spanish VACH cohort. *J Antimicrob Chemother*. 2009 Jan;63(1):189-96. Epub 2008 Nov 6.5.

Lewis W. Nucleoside reverse transcriptase inhibitors, mitochondrial DNA and AIDS therapy. *Antivir Ther*. 2005;10 Suppl 2:M13-27. Review.

Marcelin AG, Flandre P, Furco A, Wirden M, Molina JM, Calvez V; AI454-176 Jaguar Study Team. Impact of HIV-1 reverse transcriptase polymorphism at codons 211 and 228 on virological response to didanosine. *Antivir Ther*. 2006;11(6):693-9.

Masia M, Gutierrez F, Padilla S, Ramos JM, Pascual J. Severe toxicity associated with the combination of tenofovir and didanosine: case report and review. *Int J STD AIDS*. 2005 Sep;16(9):646-8. Review.

Ntemgwa ML, Toni TD, Brenner BG, Oliveira M, Asahchop EL, Moisi D, Wainberg MA. Nucleoside and nucleotide analogs select in culture for different patterns of drug resistance in human immunodeficiency viruses 1 and 2. *Antimicrob Agents Chemother*. 2008 Dec 8. [Epub ahead of print].

Torti C, Lapadula G, Barreiro P, Soriano V, Mandalia S, De Silvestri A, Suter F, Maggiolo F, Antinori A, Antonucci F, Maserati R, El Hamad I, Pierotti P, Sighinolfi L, Migliorino G, Ladisa N, Carosi G. CD4+ T cell evolution and predictors of its trend before and after tenofovir/didanosine backbone in the presence of sustained undetectable HIV plasma viral load. *J Antimicrob Chemother*. 2007 Apr 13.

Manufacturer Information

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Manufacturer Information (cont.)

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

1. AHFS Drug Information - 2008; p. 721
2. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 6, 41. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
3. FDA - Drugs Used in the Treatment of HIV Infection. Available at: <http://www.fda.gov/oashi/aids/virals.html>. Accessed 12/28/08.
4. FDA - Didanosine Generic Approval Letter. Available at: <http://www.fda.gov/cder/foi/appletter/2004/77167ltr.pdf>. Accessed 12/28/08.
5. AHFS Drug Information - 2008; p. 721
6. AHFS Drug Information - 2008; p. 722
7. HIV InSite - Didanosine. Available at: <http://hivinsite.ucsf.edu/InSite?page=ar-01-02>. Accessed 12/28/08.
8. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
9. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
10. AHFS Drug Information - 2008; p. 730
11. AHFS Drug Information - 2008; p. 730
12. AHFS Drug Information - 2008; p. 730
13. Bristol-Myers Squibb - Videx EC Prescribing Information, August 2006, p. 1. Available at: <http://www.videxec.com/products/data/index.html>. Accessed 12/28/08.
14. AHFS Drug Information - 2008; p. 730
15. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
16. Wolters Kluwer Health, Inc. - Didanosine, Facts and Comparisons 4.0. Available at: <http://online.factsandcomparisons.com>. Accessed 12/28/08.

Didanosine



17. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 24-5, 60. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
18. AHFS Drug Information - 2008; p. 730
19. AHFS Drug Information - 2008; p. 730
20. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 10, 44. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
21. Wolters Kluwer Health, Inc. - Didanosine, Facts and Comparisons 4.0. Available at: <http://online.factsandcomparisons.com>. Accessed 12/28/08.
22. AHFS Drug Information - 2008; p. 730
23. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 3, 41. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
24. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 7, 42. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
25. AHFS Drug Information - 2008; p. 729
26. AHFS Drug Information - 2008; p. 730
27. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 16, 52-3. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
28. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 17, 53. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
29. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 17, 54. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
30. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 18, 54-5. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
31. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
32. AHFS Drug Information - 2008; p. 730
33. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 16, 53. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
34. AHFS Drug Information - 2008; p. 727
35. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 12, 48. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
36. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
37. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
38. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
39. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
40. Bristol-Myers Squibb - Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 21, 57. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
41. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 12, 48. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
42. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
43. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 23, 25. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
44. AIDSinfo - Important New Clinical Data, Potential Early Virologic Failure Associated With the Combination Antiretroviral Regimen of Tenofovir Disoproxil Fumarate, Didanosine, and Either Efavirenz or Nevirapine in HIV Treatment-Naive Patients with High Baseline Viral Loads. [Dear Healthcare Provider Letter]. New York: Bristol-Myers Squibb; November 2004. Available at: <http://www.fda.gov/oashi/aids/listserv/bms.pdf>. Accessed 12/28/08.
45. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 16, 52. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50, 20155s39, 20156s40, 21183s16lbl.pdf>. Accessed 12/28/08.
46. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.

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47. Pharm GKB - The Pharmacogenetics and Pharmacogenomics Knowledge Base - didanosine. Available at: <http://www.pharmgkb.org>. Accessed 12/28/08.
48. AHFS Drug Information - 2008; p. 731
49. Wolters Kluwer Health, Inc. - Didanosine, Facts and Comparisons 4.0. Available at: <http://online.factsandcomparisons.com>. Accessed 12/28/08.
50. Wolters Kluwer Health, Inc. - Didanosine, Facts and Comparisons 4.0. Available at: <http://online.factsandcomparisons.com>. Accessed 12/28/08.
51. AHFS Drug Information - 2008; p. 731
52. AHFS Drug Information - 2008; p. 731
53. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, p. 67. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
54. FDA - HIV/AIDS List Serve Archive 2008 (September 29, 2008). Available at: <http://www.fda.gov/oashi/aids/listserve/archive.html>. Accessed 12/28/08.
55. Bristol-Myers Squibb - Didanosine Pediatric Powder for Oral Solution Package Insert, January 2007, p. 4. Available at: http://packageinserts.bms.com/pi/pi_videx.pdf. Accessed 12/28/08.
56. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 31-2, 55, 65-6. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
57. FDA - HIV/AIDS List Serve Archive 2008 (September 29, 2008). Available at: <http://www.fda.gov/oashi/aids/listserve/archive.html>. Accessed 12/28/08.
58. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, 01/21/04, pp. 31, 66. Available at: http://www.fda.gov/cder/foi/label/2004/20154slr044,20155slr034,20156slr035,21183s010_videx_ibl.pdf. Accessed 12/28/08.
59. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
60. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
61. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
62. Merck Index - 2006; p. 525
63. Merck Index - 2006; p. 525
64. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
65. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 6, 40. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
66. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 2, 36. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
67. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, p. 65. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
68. AHFS Drug Information - 2008; p. 731
69. Bristol-Myers Squibb - Videx EC and Videx Prescribing Information, August 2006, pp. 6, 40. Available at: <http://www.fda.gov/cder/foi/label/2006/020154s50,20155s39,20156s40,21183s16lbl.pdf>. Accessed 12/28/08.
70. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
71. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
72. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
73. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
74. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 12/28/08.
75. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 05/20/08.