# M.D./alert®

June 2006

Dear Health Care Professional:

Roche Pharmaceuticals would like to inform you that the sale and distribution of its anti-HIV medication HIVID® (zalcitabine) Tablets will be discontinued by December 31, 2006. HIVID is one of the first nucleoside reverse transcriptase inhibitors (NRTIs), which became available in 1992. While HIVID represented a significant breakthrough at that time, great progress has been made in the development of HIV treatments and newer NRTIs have generally replaced HIVID.

Current HIV treatment guidelines do not recommend HIVID and several discourage consideration of its use in favor of newer NRTIs. Furthermore, specific recommendations within treatment guidelines state that HIVID should not be administered in combination with ddI, d4T, 3TC or ZDV further limiting the ability to construct a nucleoside backbone containing HIVID. Other NRTIs are available with more favorable risk/benefit profiles, with the result that the use of HIVID has been declining since 1996 and continues to decline. Roche has elected to discontinue HIVID in view of these developments; this is not the result of any safety or efficacy issues regarding the product.

At this time, we encourage physicians to refrain from starting HIVID treatment in their HIV-positive patients. If you are aware of a patient receiving HIVID, please notify the prescribing health care provider (if someone other than yourself) and the patient regarding this announcement. We encourage you or the prescribing health care provider to discuss appropriate alternative treatment regimens with your patients currently receiving HIVID.

Having been at the forefront of HIV research since the beginning of the epidemic, Roche continues to commit significant resources to continuing research, development and partnerships in HIV. Our objective is the development of innovative new therapies to enhance the wellbeing of people living with HIV/AIDS.

Enclosed you will find the complete product information for HIVID. If you have any questions regarding the discontinuation of HIVID, please call the Roche Professional Product Information Department at 1-800-526-6367.

Please see important safety information at the close of this letter.

Sincerely,

Lars E. Birgerson, MD, PhD
Vice President, Medical Affairs

**Indication**

HIVID is indicated in combination with antiretroviral agents for the treatment of HIV infection.

**Important Safety Information**

**WARNING:**

**The use of HIVID has been associated with significant clinical adverse reactions, some of which are potentially fatal. HIVID can cause severe peripheral neuropathy and because of this should be used with extreme caution in patients with preexisting neuropathy. HIVID may also rarely cause pancreatitis and patients who develop any symptoms suggestive of pancreatitis while using HIVID should have therapy suspended immediately until this diagnosis is excluded.**

**Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including HIVID.**

**In addition, rare cases of hepatic failure and death considered possibly related to underlying hepatitis B and HIVID have been reported.**

HIVID is contraindicated in patients with clinically significant hypersensitivity to zalcitabine or to any of the excipients contained in the tablets.

Concomitant use of zalcitabine and lamivudine is not recommended. The concomitant use of HIVID with drugs that have the potential to cause peripheral neuropathy should be avoided where possible. These drugs include antiretroviral nucleoside analogues, chloramphenicol, cisplatin, dapsone, disulfiram, ethionamide, glutethimide, gold, hydralazine, iodoquinol, isoniazid, metronidazole, nitrofurantoin, phenytoin, ribavirin, and vincrisine. Concomitant use of HIVID with didanosine is not recommended. Simultaneous ingestion of zalcitabine with magnesium/aluminum-containing antacids is not recommended since the absorption of zalcitabine is moderately reduced (approximately 25%) when administered with these products.

Patients with renal impairment may be at a greater risk of toxicity from HIVID due to decreased drug clearance. Dosage adjustment is recommended in these patients. Redistribution/accumulation of body fat has been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown and a causal relationship has not been established. Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including HIVID.

Grade 2, 3 and 4 clinical adverse events that occurred in ≥ 1% of patients in a comparative monotherapy trial of HIVID vs. didanosine (ddI) and/or a comparative combination trial of zidovudine (ZDV) monotherapy vs. HIVID and zidovudine combination include fatigue, headache, fever, abdominal pain, oral lesions/stomatitis, vomiting/nausea, diarrhea/constipation, abnormal hepatic function, convulsions, peripheral neuropathy, rash/pruritus/urticaria, depression and painful/swollen joints.

HIVID is not a cure for HIV infection and does not prevent the transmission of HIV.