ddI (didanosine, Videx EC)

Summary
Videx EC (enteric-coated ddI) is a type of anti-HIV drug called a nuke or nucleoside analogue. Common side effects of ddI can include headache, nausea and rash. ddI is taken once daily on an empty stomach. The dose of ddI used depends on your weight.

What is Videx EC?
Videx EC is the brand name of an extended-release version of the anti-HIV drug ddI (didanosine).

How does ddI work?
To explain how ddI works, we need to first tell you some information about HIV. When HIV infects a cell it takes control of that cell. HIV then forces the cell to make many more copies of the virus. In order to make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced or blocked, production of HIV slows or stops.

ddI interferes with an enzyme called reverse transcriptase (RT), which is used by HIV-infected cells to make new viruses. Since ddI inhibits, or reduces the activity of this enzyme, this drug causes HIV-infected cells to slow down or stop production of new viruses.

How do people with HIV use ddI?
ddI is used in combination with several other anti-HIV drugs, including nukes (nucleoside analogues), and drugs from other groups or classes of drugs such as non-nukes (NNRTIs) and protease inhibitors (PIs). Combinations such as these are called antiretroviral therapy, or ART. For more information on ART, see CATIE’s Your Guide to HIV Treatment.

For many people with HIV, the use of ART has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to reduce the risk of developing a life-threatening infection.
Neither ddl nor any other anti-HIV medication is a cure for HIV. It is therefore important that you do the following:

- See your doctor regularly so that he/she monitors your health.
- Continue to practise safer sex and take other precautions so as not to pass HIV on to other people and protect yourself from different strains of HIV and other germs.

**Warnings**

1. **Pancreatitis**

Painfully swollen pancreas glands have been reported in some people taking ddl as part of ART. Symptoms of pancreatitis can include the following:

- abdominal pain, particularly when laying down
- nausea
- vomiting
- unexpected sweating
- fever
- anxiety

If left untreated, pancreatitis can be fatal. **If you think that you may have pancreatitis, consult your doctor right away.**

The risk for pancreatitis may be increased in people who:

- have a CD4+ count less than 200
- have higher-than-normal levels of triglycerides in the blood
- have kidney problems
- drink alcohol
- use another nuke called d4T ( stavudine, Zerit)
- use intravenous pentamidine

2. **Lactic acidosis**

Higher-than-normal levels of lactic acid can occur in the blood. This condition is called lactic acidosis and has happened in some people who have used nukes, including ddl. Women who are overweight are at increased risk for lactic acidosis. Sometimes the livers of people with lactic acidosis become swollen because of fatty deposits. Signs and symptoms of lactic acidosis may include the following:

- nausea
- vomiting
- abdominal pain
- diarrhea
- unexpected tiredness
- unexpected muscle pain
- feeling cold especially in the arms and legs
- feeling dizzy or light-headed

If these symptoms persist, see your doctor right away.

3. **Nerve damage in the eyes**

ddl may also affect the nerves in your eyes. You may develop changes in your vision, such as seeing abnormal colours or blurred vision. It is therefore important that you have regular eye examinations. As well, if you notice any changes to your vision, tell your doctor right away.

4. **Liver health**

People with pre-existing liver damage may need to be monitored for signs and symptoms of ddl toxicity. Liver enzyme levels in the blood may rise when taking ddl.

Recently, preliminary reports from Europe suggest that in rare cases, ddl may be associated with liver damage. These reports arise from HIV-positive people who are not infected with hepatitis-causing viruses but who were using ART. Features held in common by affected people were as follows:

- all had higher-than-normal levels of liver enzymes
- there were no obvious causes of liver problems
• no hepatitis-causing viruses were detected
• none of the participants were alcoholics
• swollen blood vessels in the throat and abdomen
• bleeding in the throat or abdomen
• water retention in the abdomen
• unintentional weight loss
• black stools
• exposure to ddl for at least two years

If you are using ddl and develop any of these symptoms, talk to your doctor right away. According to European doctors who reported these findings, switching patients from ddl to an appropriate replacement resulted in symptoms clearing.

Some people taking ddl may develop portal hypertension (high blood pressure in the large vein of the liver). This can be very serious and your doctor may conduct various tests to check for this condition.

5. Tenofovir

Tenofovir is another anti-HIV drug and is sold under the brand name Viread. Tenofovir can also be found in the following medications:
• Truvada
• Atripla

Tenofovir raises levels of ddl in the blood. This can increase the risk of ddl-related side effects including the following, some of which can be fatal:
• lactic acidosis
• pancreatitis
• peripheral neuropathy

People taking tenofovir and ddl need to have their dose of ddl reduced. Speak to your HIV specialist about the dose of ddl that is right for you. Bristol-Myers Squibb, the manufacturer of ddl, warns that the use of both ddl and tenofovir should be done with caution.

Side effects

1. General side effects

Side effects that have occurred in ddl users include the following:
• headache
• nausea
• vomiting
• diarrhea
• rash

2. Peripheral neuropathy

Peripheral neuropathy—damage to the nerves in the hands, feet and/or legs—can occur in people taking ddl. When a person has peripheral neuropathy, they usually experience one or more of the following symptoms in their hands, feet and/or legs:
• pain
• numbness
• tingling
• shooting pains
• burning

If you have had peripheral neuropathy in the past, let your doctor know before you start taking ddl. While taking ddl, if you notice any of these symptoms of PN, tell your doctor immediately. Taking the nuke d4T (stavudine, Zerit) with ddl can increase the risk of peripheral neuropathy.

3. Pregnancy

There are no well-controlled studies of ddl in pregnant HIV-positive women. Therefore, the manufacturer recommends that ddl “should be used in pregnant women only if the potential benefits outweigh the potential risks.”
4. Lipodystrophy syndrome

The HIV lipodystrophy syndrome is the name given to a range of symptoms that can develop over time when people use ART. Some features of the lipodystrophy syndrome include:

- loss of fat just under the skin (subcutaneous fat) in the face, arms, and legs
- bulging veins in the arms and/or legs due to the loss of fat under the skin
- increased waist and belly size
- fat pads at the back of the neck (“buffalo hump”) or at the base of the neck (“horse collar”)
- small lumps of fat in the abdomen
- increased breast size (in women)

Together with these physical changes, lab tests of your blood may detect the following:

- increased levels of fatty substances called triglycerides
- increased levels of LDL-cholesterol (low-density lipoprotein), or “bad” cholesterol
- increased levels of sugar (glucose)
- increased levels of the hormone insulin
- decreased sensitivity to insulin (insulin resistance)
- decreased levels of HDL-cholesterol (high-density lipoprotein), or “good” cholesterol

The precise causes of the HIV lipodystrophy syndrome are not clear and are difficult to understand because in some people with HIV, there may be one or more aspects of the syndrome taking place. For instance, some people may experience fat wasting, others fat gain, and others may experience both fat gain and wasting. What is becoming increasingly clear is that unfavourable changes in the lab readings of glucose, cholesterol and triglycerides over a period of several years increase the risk of diabetes and cardiovascular disease. So far, however, the many benefits of ART are much greater than the increased risk of cardiovascular disease or other side effects.

Maintaining a normal weight, eating a healthy diet, exercising regularly and quitting smoking are all important in helping you to reduce your risk of diabetes, heart disease and other complications. Regular visits to your doctor for checkups and blood tests are a vital part of staying healthy. If necessary, your doctor can prescribe lipid-lowering therapy.

Researchers are studying the lipodystrophy syndrome to try to discover ways of helping people with HIV avoid or reduce this problem. To find out more about options for managing aspects of the lipodystrophy syndrome, see CATIE’s Practical Guide to HIV Drug Side Effects.

Drug interactions

Always consult your doctor and pharmacist about taking any other prescription or non-prescription medication, including herbs, supplements and street drugs.

Some drugs can interact with ddI, increasing or decreasing its levels in your body. Increased drug levels can cause you to experience side effects or make pre-existing side effects worse. On the other hand, if drug levels become too low, HIV can develop resistance and your future treatment options may be reduced.

It may also be necessary to avoid drugs that do not affect levels of the medications contained in ddI, but cause similar side effects.

If you must take a drug that has the potential to interact with your existing medications, your doctor can do the following:

- adjust your dose of either your anti-HIV drugs or other medications
- prescribe different anti-HIV drugs for you

Drug interactions with ddI

The following lists contain drugs that interact or have the potential to interact with ddI. These lists are not exhaustive.
1. The manufacturer of ddl recommends that it not be used with the following drugs:
   - allopurinol (Zyloprim)
   - ribavirin

2. Use caution with these drugs
   Taking ddl with these drugs increases the risk of ddl-related toxicities such as nerve damage, pancreatitis or lactic acidosis:
   - tenofovir (Viread) or medicines containing tenofovir such as Atripla and Truvada
   - d4T (stavudine, Zerit)
   - alcohol
   - ganciclovir (Cytovene, Valcyte)
   - intravenous pentamidine
   - some anti-cancer drugs

3. Atazanavir (Reyataz)
   Some ddl users may also take the protease inhibitors atazanavir (Reyataz) and ritonavir (Norvir) as part of combination therapy. In such cases the drugs should be taken separately, ddl on an empty stomach and atazanavir/ritonavir with food.

4. Tipranavir (Aptivus)
   Some ddl users may also take the protease inhibitors tipranavir (Aptivus) and ritonavir. In such cases tipranavir/ritonavir should be taken at least 2 hours apart from ddl.

Resistance and cross-resistance
   Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes are called mutations and can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you. Combining ddl with at least two other anti-HIV drugs delays the development of drug resistance.

   To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed and directed. If doses are delayed, missed, or not taken as prescribed, levels of ddl in the blood may fall too low. If this happens, resistant virus can develop. If you find you are having problems taking your medications as directed, speak to your doctor and nurse about this. They can find ways to help you.

   When HIV becomes resistant to one drug in a class, it sometimes becomes resistant to other drugs in that class. This is called cross-resistance. Feel free to talk with your doctor about your current and future treatment options. To help you decide what these future therapies might be, at some point your doctor can have a small sample of your blood analysed using resistance testing.

   Should HIV in your body become resistant ddl, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

   Here are some additional points to note:
   - ddl should not be used as part of a triple nuke regimen as this has not been proven to be effective against HIV.
   - Also, reports of treatment failure have occurred among people new to HIV therapy who had high viral loads and were treated with a combination of ddl, tenofovir and a non-nuke.

Dosage and formulations
   Enteric coated ddl (Videx EC) is available as capsules, in the following strengths:
   - 125 mg
   - 200 mg
   - 250 mg
   - 400 mg

   The adult dosage of ddl depends on your weight as follows:
   - people who weigh 60 kg (132 pounds) or more – 400 mg once daily
   - people who weigh less than 60 kg – 250 mg once daily
Note that ddI should be taken 1.5 hours before or 2 hours after eating.

All medications should always be taken as prescribed and directed.

**Availability**

Enteric coated ddI is licensed in Canada for the treatment of HIV infection in adults, in combination with other anti-HIV drugs. Your doctor can tell you more about the availability and coverage of enteric coated ddI in your region. CATIE’s online module Federal, Provincial and Territorial Drug Access Programs also contains information about Canadian drug coverage.

**References**


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**Disclaimer**

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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