

Emtricitabine (FTC, Emtriva)

information on the nucleoside analogue
reverse transcriptase inhibitor used to treat hiv disease

The Food and Drug Administration (FDA) approved emtricitabine in July 2003 for use by adults in combination with other anti-HIV drugs. Emtricitabine is a *nucleoside analogue reverse transcriptase inhibitor* (NRTI). Other drugs in this class include abacavir, Combivir, didanosine, didanosine EC, lamivudine, stavudine, stavudine XR, Trizivir, zalcitabine, and zidovudine.

Who should use it?

Emtricitabine is very similar to lamivudine. It may prove to be a valuable tool for people across the spectrum of HIV treatment. Thus far it has shown relatively few side effects. The advantage of emtricitabine's once daily dosing may appeal to those trying to simplify their regimens.

What does the research show?

Several studies support the approval of emtricitabine. One included 571 people who had never taken anti-HIV drugs. Volunteers received didanosine and efavirenz with either emtricitabine or stavudine. After 48 weeks (nearly one year), 81% of those receiving emtricitabine reached

undetectable viral loads compared to 68% on stavudine. CD4+ cell counts increased about the same between the groups, though slightly higher for emtricitabine recipients. More people on stavudine quit the study because of side effects—22% on stavudine vs. 15% on emtricitabine.

In another study, 440 people used either emtricitabine (once daily) or lamivudine (twice daily) with other anti-HIV drugs. Before study entry, all were on effective, standard therapy including lamivudine along with other anti-HIV drugs for at least 12 weeks. People stayed on their regimens but were randomly assigned to either continue on lamivudine or switch to emtricitabine. After 48 weeks, outcomes were similar. Although not statistically significant, slightly more people had undetectable viral load among those who stayed on lamivudine. Side effects were fairly similar between the groups.

In general, results from these two large studies suggest that emtricitabine may be slightly more active and have fewer side effects than stavudine. Emtricitabine appears to have similar activity and with perhaps only slightly more side effects as lamivudine.

How to use it?

Emtricitabine is a 200mg pill, taken once daily, with or without food. Its once daily dosing makes it attractive to use. Dose changes are likely needed for people with kidney complications, including those on dialysis.

What about side effects?

Emtricitabine has relatively few side effects that occur rarely. The most common ones include headache, diarrhea, nausea and rash.

Only 1% quit the studies due to these side effects. Generally speaking, side effects were similar for emtricitabine as for other regimens, like ones with stavudine or lamivudine. A noted exception was skin discoloration of the palms of hands and/or soles of feet among those on emtricitabine. There were no other symptoms related to this discoloration, and researchers aren't sure what caused this side effect.

In addition to being active against HIV, emtricitabine appears to be active against hepatitis B virus (HBV). People with both HIV and HBV have faced a worsening of HBV-related complications after stopping emtricitabine. For this reason, it's recommended that people living with both HIV and HBV use caution when taking emtricitabine, as it has not been tested well in this setting. Moreover, careful monitoring of HBV should follow after stopping emtricitabine.



Lactic acidosis and liver problems

A relatively rare but serious side effect from using NRTIs is severe chemical imbalances in the body called *lactic acidosis*. It may be more of a concern with stavudine and stavudine + didanosine. In addition to abnormal lab results, symptoms of lactic acidosis include severe nausea, vomiting, muscle weakness and shortness of breath. One result of the build-up of lactic acid in the blood is liver problems, including enlargement (*hepatomegaly*) with fat deposits (fatty liver or *steatosis*). This could result in liver failure and death.

People who are overweight and those who have used NRTIs for a long time are at greater risk for this side effect. Women, particularly overweight women, appear to have a greater risk than men. The risk for severe and possibly fatal lactic acidosis appears to be greater among pregnant women taking stavudine and/or didanosine.

For more information on lactic acidosis, read Project Inform's publication, *Mitochondrial Toxicity*. Also, the use of anti-HIV drugs have been linked to changes in body shape and fat distribution. NRTIs may be particularly associated with loss of fat, such as facial or limb wasting. For more information, read Project Inform's publication, *Lipodystrophy*, available at 1-800-822-7422 or www.projectinform.org.

HIV and the brain

Because HIV can infect brain cells, it's important to consider a drug's ability to reach the brain when putting together an anti-HIV regimen. It's probably wise to include at least one drug that has been shown to cross the blood-brain barrier to some useful degree as part of your regimen. These include abacavir, amprenavir, atazanavir, nevirapine, stavudine, zidovudine and to a lesser degree indinavir and lamivudine. Efavirenz has not been shown to cross the barrier to a significant degree, but some experts speculate that it might have some useful effect in impacting HIV in the spinal fluid.



What about drug resistance?

Drug resistance occurs when HIV changes or *mutates* and the drug no longer controls its reproduction. Resistance to emtricitabine may be slow to develop when used together with other anti-HIV drugs. However, HIV resistance to emtricitabine has been seen.

Cross-resistance occurs when resistance to one drug makes other drugs less effective. Studies suggest that once HIV has developed resistance to emtricitabine, then lamivudine and zalcitabine may be less effective. Emtricitabine and lamivudine share similar resistance patterns, so virus resistant to lamivudine will likely be resistant to emtricitabine as well. Test tube studies suggest that HIV showing certain types of resistance to abacavir, didanosine, tenofovir or zalcitabine may also be less susceptible to emtricitabine.

What about drug interactions?

It's not expected that emtricitabine will have many drug interactions. Studies have been conducted with a few other anti-HIV drugs and no interactions were observed. Whether or not emtricitabine interacts with other medications (methadone, psychiatric medicines, street drugs, etc.) is not known. There are possible interactions with other drugs that are cleared through the kidneys. People are encouraged to discuss these interactions among ALL of the therapies and substances they are taking with their doctor and/or pharmacist.

What is known about this drug for women, people of color, children, the elderly?

Emtricitabine has not been studied in pregnant women. Thus, it's not recommended for either pregnant or nursing women. It is not known if emtricitabine is found in breast milk. Because HIV can be passed through breast milk, nursing is generally discouraged in areas where alternatives exist. Early results from animal studies do not suggest that there will be a problem with emtricitabine during pregnancy. However, animal studies do not always predict safety in humans.

Studies including men, women and mixed racial and ethnic populations do not suggest differences in the rate at which their bodies process and clear emtricitabine based on gender, race or ethnicity. Emtricitabine has not been well researched in children. Not enough people over the age of 65 were included to provide unique information for the elderly to consider.

How do I get it?

Emtricitabine is available by prescription. Many states will likely cover emtricitabine through their AIDS Drug Assistance Programs (ADAP). To find out if you're eligible for your state ADAP and if emtricitabine is covered through your state's program, contact Project Inform at 1-800-822-7422. Information is also available from AIDS Treatment Data Network at 1-800-734-7104 or www.atdn.org. People who lack insurance, Medicaid, ADAP coverage or other ways to buy the drug might gain access to it through the company's Patient Assistance Program at 1-800-445-3235.

drug i.d. chart

GENERIC NAME	TRADE NAME
Protease inhibitor	
amprenavir	Agenerase
atazanavir	Reyataz
fosamprenavir	Lexiva
indinavir	Crixivan
lopinavir + ritonavir	Kaletra
nelfinavir	Viracept
ritonavir	Norvir
saquinavir hgc	Invirase
saquinavir sgc	Fortovase
Nucleoside (NRTI) and nucleotide (NtRTI) analogue reverse transcriptase inhibitor	
abacavir	Ziagen
didanosine (ddI)	Videx
didanosine enteric-coated (ddI EC)	Videx EC
emtricitabine (FTC)	Emtriva
lamivudine (3TC)	Epivir
stavudine (d4T)	Zerit
stavudine extended release (d4T XR)	Zerit XR
tenofovir	Viread
zalcitabine (ddC)	Hivid
zidovudine (AZT)	Retrovir
3TC/AZT	Combivir
3TC/AZT/abacavir	Trizivir
Non-nucleoside reverse transcriptase inhibitor (NNRTI)	
delavirdine	Rescriptor
efavirenz	Sustiva
nevirapine	Viramune
Fusion inhibitor	
enfuvirtide (T20)	Fuzeon

commentary

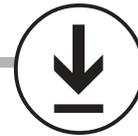
Some consider emtricitabine to be a “me too” NRTI: just another drug in a growing list with no special benefits. Data suggesting that emtricitabine is superior to stavudine may have been important a year or so ago when stavudine was among the most used and seemingly favored NRTI among patients and providers. However, the use of stavudine has waned because of its implicated role in fat loss and liver complications.

How emtricitabine compares to lamivudine is perhaps more important. Lamivudine has long been regarded as one of the most potent NRTIs when used correctly with other potent drugs. The arrival of Combivir as a single pill, taken twice daily, made three-drug therapy immensely easier. Combivir provided two NRTIs as the backbone for a potent three-drug regimen. Doctors and patients alike sighed in relief at the new formulation that helped ease the pill burden and improve adherence.

Ultimately the question is what does emtricitabine add to the anti-HIV arsenal? It appears to be a fairly potent NRTI and similar in many ways to lamivudine. Like lamivudine, it has relatively few side effects (though slightly more than lamivudine). One nice advantage is that emtricitabine is taken just once daily. This benefit may be less critical now that more and more drugs are coming out in once daily formulations, however.

Gilead Sciences, who developed emtricitabine, also makes another anti-HIV drug called tenofovir. It is also taken once daily. It is Gilead’s goal to make them into a single pill taken once daily, allowing for a potent combination in one pill. With the new protease inhibitor atazanavir (also dosed once daily) and other advances on the horizon, it may soon be possible to construct potent three-drug regimens that need as few as one or two pills once daily.

Emtricitabine thus represents a sort of dawning of a new and important phase of refinement in HIV treatment—that is, drugs that are easier to take with fewer side effects and good potency. In and of itself it offers very little in the short-term. Its real benefits likely won’t be realized until it’s co-formulated with tenofovir. The company hopes to launch this new pill in 2005.



the bottom line on emtribitabine

Benefits:

- › Equivalent to lamivudine when used as part of a three-drug regimen.
- › Once daily dosing.
- › Relatively mild side effects.

Concerns:

- › When the virus is resistant to lamivudine it will also be resistant to emtricitabine. The reverse is also true.
- › All NRTIs carry a warning that they may contribute to lactic acidosis (a potentially fatal build-up of lactic acid), especially in overweight or pregnant women.

How to get it:

- › Gilead’s Patient Assistance Program, call 1-800-455-3235.
- › Available through hospitals and pharmacies.
- › Available through some stage AIDS Drug Assistance Programs.

www.projectinform.org



Go online around the clock and get connected to treatment information in the privacy of your own home!