

Fosamprenavir (Telzir)

Summary

Fosamprenavir is a type of anti-HIV drug called a protease inhibitor. The most common side effects of fosamprenavir can include gastrointestinal problems, headache, and rash. For the initial treatment of HIV, it is usually taken at a dose of 1400 mg (two tablets) with 200 mg (two capsules) ritonavir once daily. For treatment-experienced patients, it is usually taken at a dose of 700 mg (one tablet) twice daily with 100 mg (one capsule) ritonavir also twice daily. Both medications may be taken with or without food.

What is fosamprenavir?

Fosamprenavir, sold under the brand name Telzir (Lexiva in the US), is a type of anti-HIV drug (antiretroviral) drug called a protease inhibitor (PI). Fosamprenavir is used in combination with other anti-HIV drugs to treat (but not cure) HIV.

How does fosamprenavir work?

To explain how fosamprenavir 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. To make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced, the production of HIV slows.

Fosamprenavir belongs to a group or class of drugs called protease inhibitors. Fosamprenavir interferes with an enzyme called protease, which is used by HIV-infected cells to make new viruses. Once fosamprenavir is absorbed in the body, it is converted to its active, anti-HIV form called amprenavir. Since amprenavir inhibits, or reduces the activity of this enzyme, this drug causes HIV-infected cells to produce fewer viruses.

How do people with HIV use fosamprenavir?

Fosamprenavir is used in combination with several other anti-HIV drugs, usually nucleoside analogues, and sometimes including drugs from

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other classes such as non-nukes (non-nucleoside reverse transcriptase inhibitors). Combinations such as this are called antiretroviral therapy, or ART. For more information on ART, see *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 fosamprenavir 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 can monitor your health.
- Continue to practise safer sex and take other precautions so as not to pass HIV on to other people.

Warnings

People treated with fosamprenavir can develop higher-than-normal levels of cholesterol (hypercholesterolemia). Prolonged, elevated levels of cholesterol can be one factor that increases the risk for cardiovascular disease, including a heart attack. If you have elevated levels of cholesterol, ask your doctor about your risk for cardiovascular disease and ways to reduce your risk.

Side effects

1. General

Common side effects that have been reported by some fosamprenavir users include the following:

- nausea
- abdominal pain
- vomiting
- diarrhea
- headache
- lack of energy

Most of these side effects were either mild or moderate in severity. Also, if they did occur,

these side effects happened early in the course of fosamprenavir therapy.

2. Abnormal laboratory results

Between 4% and 8% of fosamprenavir users have developed severely or dangerously elevated levels of the following in their blood:

- ALT (alanine aminotransferase or SGPT) – a liver enzyme
- AST (aspartate aminotransferase or SGOT) – a liver enzyme
- lipase – an enzyme produced by the pancreas gland
- triglycerides – a fatty substance

The reasons for increased levels of these substances are not clear. In some cases they may suggest liver damage (in the case of liver enzymes), an inflamed pancreas gland (elevated lipase) or an increased risk for cardiovascular disease (high triglycerides). It is important to discuss your lab test results with your doctor(s) and nurse.

3. Rash

Rash can be a side effect of fosamprenavir. However, this is usually mild and can clear within two or three weeks. However, in cases of severe rash, or rash of moderate intensity that is accompanied by other symptoms, it is important to contact your doctor right away because fosamprenavir must be discontinued.

In clinical trials, less than 1% of fosamprenavir users developed a severe or life-threatening rash (Stevens-Johnson syndrome).

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 *A 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 fosamprenavir, 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.

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 fosamprenavir

Below are lists of actual and potential drug interactions. These lists are not exhaustive. The manufacturer recommends that the following drugs should **not** be taken by fosamprenavir users, because this could lead to serious (or life-threatening) reactions:

- anesthetics – lidocaine
- antidepressants – tricyclic antidepressants such as imipramine, amitriptyline
- antihistamines – astemizole (Hismanal), terfenadine (Seldane)
- anti-malaria drugs – halofantrine (Halfan)
- anti-psychotic drugs – pimozide (Orap)
- blood thinning agents – warfarin (Coumadin)

- gastrointestinal motility agents – cisapride (Prepulsid)
- drugs for abnormal heart rhythms – amiodarone (Codarone), bepridil (Vascor), flecainide (Tambocor), propafenone (Rythmol), quinidine, lidocaine (systemic)
- migraine medications (ergot derivatives) – dihydroergotamine (Migranal), ergotamine (Ergomar), ergonovine
- anti-anxiety agents – midazolam (Versed), triazolam (Halcion), diazepam (Valium), flurazepam (Dalmane)
- drugs to treat benign prostatic hyperplasia (BPH) – alfuzosin (Xatral)

The following drugs can *increase* levels of fosamprenavir in the blood:

- HIV protease inhibitors – indinavir (Crixivan)
- HIV nukes – AZT (zidovudine), abacavir (Ziagen)
- HIV non-nukes – efavirenz (Sustiva)
- antibiotics – clarithromycin (Biaxin)
- anti-fungal agents – ketoconazole (Nizoral), itraconazole (Sporanox)

The following drugs can *decrease* levels of fosamprenavir in the blood:

- antibiotics/anti-tuberculosis medications – rifampin, rifampicin. These drugs should not be used with fosamprenavir
- herbs – St. John's wort (hypericin, hyperforin)
- anti-ulcer medications – (histamine H₂ receptor antagonists) such as cimetidine (Tagamet), ranitidine (Zantac)
- anti-seizure medications – phenytoin (Dilantin), carbamazepine (Tegretol), phenobarbital

Fosamprenavir can *increase* levels of the following drugs in the blood:

- antibiotics – clarithromycin, dapsone, erythromycin, rifabutin (Mycobutin). If rifabutin must be used, then the dose of this drug should be reduced by at least 75%. Regular

blood tests are necessary to ensure that bone marrow damage does not occur.

- anti-fungal agents – itraconazole (Sporanox), ketoconazole (Nizoral)
- erectile dysfunction (ED) medications – sildenafil (Viagra), vardenafil (Levitra) and tadalafil (Cialis). When taken by users of fosamprenavir, these medications can reach very high levels in the blood, causing dangerous side effects. If you have difficulty getting or maintaining an erection speak to your doctor about how you might safely use these ED medications.
- lipid-lowering medications commonly called statins – lovastatin (Mevacor) and simvastatin (Zocor) are not recommended for use by people taking fosamprenavir. When using other statins such as atorvastatin (Lipitor), the lowest possible dose should be used and should not exceed 20 mg. Other statins such as fluvastatin (Lescol) and pravastatin (Pravachol) may be considered.
- transplant medications – levels of the following may be increased in users of fosamprenavir/r: cyclosporine (Neoral), rapamycin (Sirolimus, Rapamune), tacrolimus (Prograf).

Fosamprenavir can *decrease* the levels of the following drugs:

- antidepressants – paroxetine (Paxil), trazodone
- narcotics – methadone; monitoring for signs of methadone withdrawal and adjusting the dose may become necessary in some people also using fosamprenavir
- hormones – estrogens, proestrogens and some glucocorticoids may interact with fosamprenavir. Use of the steroid fluticasone (Advair, Flonase, Flovent) should be avoided by fosamprenavir users.

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 fosamprenavir 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 fosamprenavir 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 to fosamprenavir, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

Dosage and formulations

Fosamprenavir is available as 700 mg tablets and in a liquid formulation.

Fosamprenavir is not well absorbed on its own and it is almost always taken in combination with another drug, called ritonavir (Norvir), which 'boosts' the absorption of fosamprenavir. This combination of drugs is written as fosamprenavir/r.

For adults, there are several doses and schedules that may be used when taking fosamprenavir/r. For instance, in people who have never used protease inhibitors and who are new to therapy, fosamprenavir/r may be taken once daily at a dose of 1400 mg fosamprenavir (two tablets) with 200 mg ritonavir (two capsules).

For treatment-experienced people with HIV, the recommended dose of fosamprenavir/r is 700 mg fosamprenavir (one tablet) twice daily, along with 100 mg ritonavir (one capsule) also twice daily. Both medications can be taken with or without food.

Formulations can change, and dosages may need to be customized. All medications should always be taken as prescribed and directed.

Availability

Fosamprenavir 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 fosamprenavir in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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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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