Tipranavir (Aptivus)

Summary
Tipranavir is a type of anti-HIV drug called a protease inhibitor. It is used only in people who have developed resistance to other protease inhibitors. Common side effects of tipranavir can include diarrhea, nausea and vomiting, stomach pain, lack of energy and headaches. It is usually taken at a dose of 500 mg together with 200 mg ritonavir (Norvir). Both drugs are taken twice daily with food.

What is tipranavir?
Tipranavir, sold under the brand name Aptivus, is a type of anti-HIV drug (antiretroviral) called a protease inhibitor (PI). Tipranavir is used in combination with other anti-HIV drugs to treat (but not cure) HIV. Tipranavir was specifically developed to be effective in treatment-experienced people (those who have already been on other anti-HIV drugs, in particular, protease inhibitors).

How does tipranavir work?
To explain how tipranavir 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.

Tipranavir belongs to a group or class of drugs called protease inhibitors. Tipranavir interferes with an enzyme called protease, which is used by HIV-infected cells to make new viruses. Since tipranavir inhibits, or reduces the activity of this enzyme, this drug causes HIV-infected cells to slow down or stop producing new viruses.

How do people with HIV use tipranavir?
Tipranavir is used in combination with several other anti-HIV drugs, usually nukes (nucleoside analogues), and sometimes including drugs from other classes such as non-nukes (NNRTIs). Combinations such as this are called antiretroviral therapy, or ART. For more information on ART, see CATIE’s Your Guide to HIV Treatment.
Tipranavir is approved for use in treatment-experienced HIV-positive adults who are resistant to other protease inhibitors (see “Resistance and cross resistance” below).

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 tipranavir 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 to protect yourself from infection with different strains of HIV and other germs.

**Warnings**

1. **Bleeding in the skull**

   There have been reports of bleeding inside the skull (intracranial hemorrhage) in people who have used tipranavir. No other abnormal bleeding has been seen in people on tipranavir. Tipranavir should be used cautiously or avoided in people at risk for excessive bleeding, such as hemophiliacs, people with injuries or who have recently had surgery, people taking drugs that increase the risk of bleeding (for example, warfarin Coumadin) or who have a health condition that increases the risk of bleeding (for example, lower-than-normal levels of platelets in the blood).

   At least 14 cases of intracranial hemorrhage had been reported among 6,840 people who were receiving tipranavir in clinical trials. Eight of these cases were fatal. More than half of the reports were from people who were also taking blood thinners or anti-clotting agents that may have contributed to the bleeding.

2. **Liver damage**

   Hepatitis and liver failure have also been reported in some people taking tipranavir. Although it has not been shown that tipranavir was definitely the cause, tipranavir is not recommended for people who already have moderate to severe liver problems. It should be used very cautiously in people with chronic hepatitis B or hepatitis C infection.

**Side effects**

1. **General**

   Common side effects that have been reported by some tipranavir users include diarrhea, nausea and vomiting, stomach pain, lack of energy and headaches. In clinical trials so far, these side effects were about as frequent with tipranavir as they were with other protease inhibitors.

2. **Rash**

   In clinical trials, rash occurred in 14% of women and 8 to 10% of men taking tipranavir. The risk of tipranavir-related rash increased in people with HIV with low CD4+ counts.

3. **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
The precise cause(s) 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 over-the-counter drugs, herbs, supplements, and street drugs.

Some drugs can interact with tipranavir, 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 tipranavir drug levels, 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 tipranavir**

The following lists contain drugs that interact or have the potential to interact with tipranavir. These lists are not exhaustive.

The manufacturer recommends that the following drugs should **not** be taken by people using tipranavir because this could lead to serious (or life-threatening) interactions.

- drugs for abnormal heart rhythms – amiodarone (Cordarone), bepridil (Vascor), flecainide (Tambocor), propafenone (Rhythmol), quinidine (Quiniglute, Quinidex)
- antihistamines – astemizole (Hismanal), terfenadine (Seldane)
- anti-migraine drugs (ergot derivatives) – dihydroergotamine (Migranal), methylergonovine, ergonovine (Ergotrate), ergotamine (Ergomar)
- Antibiotics – rifampicin (Rifadin)
- gastrointestinal motility agents – cisapride (Prepulsid)
- antipsychotics – pimozide (Orap)
- sedatives/sleeping pills – midazolam (Versed), triazolam (Halcion)
- erectile dysfunction drugs – vardenafil (Levitra); if you have erectile dysfunction, speak with your doctor about how to safely use these medications
The use of tipranavir with lovastatin (Mevacor) or simvastatin (Zocor) is not recommended. The following drugs can increase levels of tipranavir in your body:

- lipid-lowering drugs – atorvastatin (Lipitor)
- anti-fungal drugs – itraconazole (Sporanox), ketoconazole (Nizoral), fluconazole (Diflucan)

The following drugs can decrease levels of tipranavir in the blood:

- herbals – St. John’s wort

Tipranavir can increase levels of the following drugs:

- anti-fungal drugs – itraconazole (Sporanox), ketoconazole (Nizoral)
- antibiotics – clarithromycin (Biaxin), rifabutin (Mycobutin). The manufacturer recommends a 75% decrease in rifabutin dosage to 150 mg every other day.
- antidepressants – desipramine (Norpramin), fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft), trazodone
- lipid-lowering drugs – atorvastatin (Lipitor)
- anti-asthma drugs – fluticasone (Flovent), budesonide
- erectile dysfunction drugs – sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra); if you have erectile dysfunction, speak with your doctor about how to safely use these medications
- narcotics – meperidine (Demerol) is processed by the body into normeperidine. Tipranavir raises the levels of normeperidine to dangerous levels. The manufacturer does not recommend long-term use of meperidine in tipranavir users.

Tipranavir can decrease levels of the following drugs:

- HIV nukes – AZT (zidovudine, Retrovir), abacavir (Ziagen), ddI (Videx)
- HIV protease inhibitors – fosamprenavir (Telzir), lopinavir (Kaletra), saquinavir (Invirase), atazanavir (Reyataz). Tipranavir should not be used with these drugs.
- narcotics – methadone; monitoring for signs of methadone withdrawal and adjusting the dose may become necessary in some people also using tipranavir
- hormones – ethinyl estradiol (found in hormone-based birth control)
- certain antacid drugs – omeprazole (Losec, Prilosec), esomeprazole (Nexium)

Vitamin E supplements can increase the risk of intracranial hemorrhage when taken with tipranavir.

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.

Tipranavir is specifically intended for people who have used many other anti-HIV treatments and whose HIV has become resistant to other protease inhibitors.

Combining tipranavir 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 tipranavir 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 tipranavir, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.
Dosage and formulations

Tipranavir is available as 250 mg capsules. The standard adult dose of tipranavir is 500 mg (2 capsules), taken with 200 mg (two 100 mg capsules) ritonavir (Norvir), twice daily with food. The ritonavir works to boost tipranavir levels in the blood; tipranavir is not recommended for use without ritonavir.

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

Availability

Tipranavir 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 tipranavir in your region. CATIE’s online module Federal, Provincial and Territorial Drug Access Programs also contains information about Canadian drug coverage.

References


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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