

## Non-nukes

Created 10 Jul 2006 - 1:07am

Non-nucleosides are a powerful option for treating HIV, but cross-resistance can mean you only get one bite of the cherry. This is the final instalment in a three-part series looking at key [drug classes](#) [1]A group of anti-HIV drugs with the same target of action. Anti-HIV drug classes include *nucleoside analogue reverse transcriptase inhibitors*,

Non-nucleoside analogue reverse transcriptase inhibitors (also called NNRTIs or non-nukes) are a group of anti-HIV drugs with something of an equivocal character.

They include some of the most powerful weapons we have against HIV – **potent** drugs with a strong track record in suppressing the [virus](#) [2]A small infective organism which is incapable of reproducing outside a host cell. to very low levels. But this power comes at a price: **cross-resistance** between drugs is stronger within this class than in any other group, and there are just three drugs currently available to choose from.

Because of this, it's important to understand the issues associated with these medicines if you're taking them, to avoid treatments failure which could mean losing access to the entire non-nuke class.

The shift to combination treatment for HIV in the mid-1990s, widely referred to as 'the protease moment', could equally have been called 'the non-nucleoside moment'. It was the emergence of new drugs in new classes which made it possible to start turning the tide in the battle against HIV.

The first non-nuke to be approved in Australia was nevirapine (Viramune), which was listed on the [PBS](#) [3] [Pharmaceutical Benefits Scheme] The federal government program which subsidises medication costs in Australia. Anti-HIV drugs are part of a special part of the PBS called Section 100 (S100) which is used for expensive, highly specialised drugs. in late 1997. Delavirdine (Rescriptor) followed a few months later, and efavirenz (Stocrin) in 1999. That means it's been seven years since the last non-nuke was approved in Australia. Drug companies are working on new 'next-generation' non-nukes, however none of these are expected to become available in the very near future. For the foreseeable future, we have to work with what we've got.

Like nucleosides (the drug class which includes AZT, 3TC, FTC, abacavir and several others), non-nukes work by

Taking a non-nuke based treatments regimen typically means taking one non-nuke and two nucleosides; other combinations, such as combining non-nukes with protease inhibitors, have been tried but aren't usually recommended except in special circumstances.

### Choosing a non-nuke

There are three non-nucleoside drugs currently approved in Australia. But one of these, **delavirdine** (Rescriptor), is not widely prescribed due to its high pill burden, greater incidence of side effects and because it has been shown in some studies to be less effective than other drugs in the non-nuke class. If you're currently taking delavirdine you should continue to do so, however if you are starting non-nucleoside therapy your doctor will usually recommend one of the other drugs in the class.

**Nevirapine** (Viramune) was the first non-nucleoside approved in Australia. [Clinical](#) [4]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. studies have shown that combinations based around nevirapine are as effective as protease inhibitor based regimens.

Nevirapine can be taken once or twice a day, however it's usually recommended to follow the twice-daily dosing. That means one tablet taken morning and night. There are no special dietary requirements for taking this drug, so it can be taken with or without food.

The most common [side effect](#) [5]Any undesired actions or effects of a drug or treatment. Negative or adverse effects may include headache, nausea, hair loss, skin irritation, or other physical problems. Experimental drugs must be evaluated for both immediate and long-term side effects. experienced by people taking nevirapine is a

**rash**, usually appearing in the first few weeks on treatment. About 16 percent of people in clinical trials had this side effect, and it appears to be more common in women than men.

Your doctor may recommend starting treatment with a reduced dose and gradually increasing the dosage over a two-week period (**ramping up**) as this can help prevent the rash occurring. Antihistamines can sometimes help with this side effect, but should only be taken with your doctor's approval. In rare cases, the rash can be serious enough to require stopping treatment, so you should see your doctor if you have a rash, especially if it is accompanied by fever, blistering or other symptoms.

Starting treatment with nevirapine and other drugs known to cause skin rash can make it difficult to determine the cause if a rash does appear, so this should be avoided if possible. In particular, it's not recommended to start on abacavir and nevirapine at the same time, because any rash that occurs could indicate a potentially life-threatening hypersensitivity reaction.

Nevirapine can also cause problems with [liver](#) [6] **A large organ, located in the upper right abdomen, which assists in digestion by metabolising carbohydrates, fats and proteins, stores vitamins and minerals, produces amino acids, bile and cholesterol, and removes toxins from the blood.** **toxicity** – again, usually in the first few weeks after starting treatment. If you start nevirapine your doctor will want to do regular blood tests to measure liver function. Although this problem is usually only short-term, nevirapine may not be the best option for people coinfecting with hepatitis B or C. Again, this side effect occurs more often in women than men.

**Efavirenz** (Stocrin) is the other main drug in the non-nuke class. Taken in combination with an appropriate nucleoside backbone, it has been shown in clinical trials to be as effective as, or more effective than, protease inhibitor based regimens, either as first-line or second-line therapy. In head-to-head studies, efavirenz has been shown to be slightly more effective, and with more manageable side effects, than nevirapine.

Efavirenz is usually taken once daily, as a single pill taken at bedtime. There are no special dietary requirements, however taking efavirenz on a full stomach can increase the severity of side effects, so it's best to take it away from meal times.

The most common side effects experienced by people taking efavirenz are **neurological disturbances** – these can include drowsiness or insomnia, vivid dreams, abnormal thinking, agitation, feeling 'stoned', impaired concentration and memory problems. As many as 50 percent of people taking efavirenz experience these side effects in the first few weeks of treatment, and in some people they may persist for much longer, although with reduced severity.

In rare cases, people taking efavirenz may develop more serious psychiatric effects, such as depression, feeling suicidal, aggressive or paranoid. While the percentage of people experiencing these problems is very small, they may be very serious and you should see your doctor if they occur or you are concerned about them. People with existing clinical depression or a history of psychiatric disorders may wish to avoid taking efavirenz.

Despite the high prevalence of these side effects, most people experience only mild to moderate symptoms, and in trials only about three percent of people ceased efavirenz due to side effects.

Efavirenz may also cause a **rash**, usually in the first few weeks on treatment. About one-quarter of people in trials developed a skin rash, however this was usually mild and resolved fairly quickly. Antihistamines may be helpful in reducing the severity of skin rash. Efavirenz may also cause increases in **liver enzymes**.

**Both nevirapine and efavirenz** have long half-lives, which means the drug is eliminated from the body very slowly. This long half-life is one of the reasons non-nukes are so effective in suppressing HIV (because blood levels of the drug take a long time to fall) but this can also encourage the development of **resistance**.

Whatever treatment you're on, it's important to take your pills regularly and on time ( **adherence**), however this is doubly important for non-nuke based regimens. Missing doses can mean the blood levels of other drugs in your regimen fall quickly while the non-nuke levels remain relatively high. This encourages the development of viral strains which are [resistant](#) [7] HIV which has mutated and is less susceptible to the effects of one or more anti-HIV drugs is said to be resistant. to the non-nuke.

If stopping treatment with any of the non-nukes, a special **'wash-out'** procedure is used to prevent the

development of resistance. This may mean continuing to take the other drugs in the regimen for two weeks after stopping the non-nuke, or switching to another treatment (usually Kaletra monotherapy) for a couple of weeks after stopping a non-nuke based regimen. You should only ever stop treatment with your doctor's guidance.

People who have become resistant to one of the existing non-nukes will usually also develop resistance to the other non-nukes (**cross-resistance**). Because of this, it makes sense to try as hard as possible to prevent resistance developing and so maintain as many treatment options as possible.

Both nevirapine and efavirenz penetrate the **Central Nervous System** (CNS), which means they are able to block HIV replication in the brain. This may make them good choices for people with HIV-associated dementia, and may prevent its development.

Women who are or may become **pregnant** can take nevirapine but should avoid efavirenz. Animal studies have suggested that efavirenz can harm the development of unborn babies.

## Non-nukes versus PIs

Whether you choose a protease inhibitor or non-nuke based regimen depends on several factors. Both options are effective in suppressing HIV, however available choices will depend on your previous treatment history and resistance profile.

Non-nukes are a good choice if you've not taken drugs from this class before, and if you're committed to always taking your pills on time. Unlike protease inhibitors, non-nukes don't cause rises in [blood fats](#) [8]A type of fat in the blood. Elevated triglyceride levels may be a side effect of some anti-HIV drugs. (in fact they can produce substantial rises in 'good' [cholesterol](#) [9]An essential component of cell membranes and nerve fibre insulation, cholesterol is important for the metabolism and transport of fatty acids and the production of hormones and Vitamin D. Cholesterol is manufactured by the liver, and is also present in certain foods. High blood cholesterol levels have been linked to heart disease and may be a side effect of some anti-HIV medications.).

While side effects for non-nukes are quite common, most people find they can manage them, even if the side effects persist for longer than the first few weeks on treatment. Unlike protease inhibitors, non-nukes don't tend to cause nausea and diarrhoea.

- [delavirdine](#)
- [efavirenz](#)
- [HIV treatments](#)
- [HIV/AIDS basics](#)
- [nevirapine](#)
- [NNRTIs](#)
- [starting treatments](#)

### Links:

[1] <http://www.napwa.org.au/glossary/term/124>

[2] <http://www.napwa.org.au/glossary/term/125>

[3] <http://www.napwa.org.au/glossary/term/121>

[4] <http://www.napwa.org.au/glossary/term/475>

[5] <http://www.napwa.org.au/glossary/term/471>

[6] <http://www.napwa.org.au/glossary/term/102>

[7] <http://www.napwa.org.au/glossary/term/109>

[8] <http://www.napwa.org.au/glossary/term/114>

[9] <http://www.napwa.org.au/glossary/term/88>