



# Antiretroviral options

Which combination is right for you?

by Dr. Harold Dion

**So you're ready to start treatment. Based on your CD4 count and viral load, you and your doctor have decided that the time is now. You're ready to make a firm commitment to antiretrovirals. But which ones? Dosage, tolerability, side effects and durability are the main factors to consider in choosing a combo that will meet your particular needs.**

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The main goals of antiretroviral (ARV) treatment are to improve quality of life, reduce the chance of HIV-related death, restore and preserve the immune system and achieve a sustained suppression of viral loads to undetectable levels.

A combo of at least three drugs, known as Highly Active Antiretroviral Therapy (HAART) is recommended to bring viral loads down and CD4 counts up in a lasting manner. Choosing the right first combo is essential because it's the one most likely to be successful. If HIV resists the first combo, subsequent ones will prove more complicated and potentially less effective.




## The options

Each ARV falls into one of four classes, based on its target — where it blocks HIV in the replication process. The classes are called nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs) and fusion inhibitors (FIs). The following tables list all the available ARVs in Canada, dosing and possible side effects. But keep in mind that the tables don't mention all the possible side effects, only the most frequent ones. Talk to your doctor and pharmacist for more details.











## The right combo for you

There are a few different recommended drug combos for people first starting HIV treatment. They're divided into two groups: preferred and alternative regimens. A first-time treatment plan should take into account your particular needs. Talk to your doctor about important factors that

## Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

NNRTI	Dosage	Possible side effects
 Delavirdine (Rescriptor <sup>®</sup> )	4 pills 3 times a day <i>or</i> 6 pills twice a day	Temporary rashes, headaches, ↑ liver enzymes
 Efavirenz (Sustiva <sup>®</sup> )	1 pill daily	Neuropsychiatric effects, dizziness, insomnia, dreams, temporary rashes, ↑ liver enzymes
 Nevirapine (Viramune <sup>®</sup> )	1 pill daily for the first 14 days, followed by 1 pill twice a day	Temporary rashes, hepatitis (liver inflammation)

## Nucleoside reverse transcriptase inhibitors (NRTIs)

NRTI	Dosage	Possible side effects
 Abacavir (Ziagen <sup>®</sup> )	1 pill twice a day <i>or</i> 2 pills daily	Hypersensitivity reactions: Call your physician or pharmacist if you experience these symptoms: Fever, discomfort, rash, GI effects. You may have to stop taking abacavir if hypersensitivity is confirmed
 Combivir <sup>®</sup> (AZT + 3TC <sup>®</sup> combo)	1 pill twice a day	Nausea initially, headaches, fatigue, muscle diseases, anemia, lactic acidosis
 Didanosine ddi (Videx <sup>™</sup> )	2 pills twice a day <i>Fasting state. Do not take at same time as indinavir.</i>	Pancreatitis, peripheral neuropathy, nausea, diarrhea, lactic acidosis
 Didanosine ddi (Videx <sup>™</sup> EC)	1 pill daily <i>Fasting state</i>	Pancreatitis, peripheral neuropathy, nausea, diarrhea, lactic acidosis
 Lamivudine 3TC <sup>®</sup>	1 pill twice a day <i>or</i> 1 pill daily (for a stronger dose)	Generally well tolerated
 Stavudine d4T (Zerit <sup>™</sup> )	1 pill twice a day	Peripheral neuropathy, lipoatrophy, pancreatitis, lactic acidosis, hyperlipidemia
 Tenofovir (Viread <sup>®</sup> )	1 pill daily	Fatigue, headaches, nausea, diarrhea, ↓ kidney function
 Trizivir <sup>™</sup> (AZT + 3TC <sup>®</sup> + abacavir combo)	1 pill twice a day	As for individual drugs
 Zalcitabine ddC (Hivid <sup>®</sup> )	1 pill three times a day	Peripheral neuropathy, stomatitis, pancreatitis, lactic acidosis
 Zidovudine AZT (Retrovir <sup>®</sup> )	3 pills twice a day	Nausea initially, headaches, fatigue, muscle disorders, anemia, lactic acidosis

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will determine if you'll stick to your meds over the long term. Factors like pill burden (how many pills you have to take daily), dosing frequency (how many times a day), dietary restrictions (taking the pills with food or not), toxicities (negative side effects of ARVs), drug interaction potential, other conditions you have and your viral load are all important when choosing ARV treatment. Together you'll arrive at the best possible combo for you.

Combo recommendations are made by physicians with HIV expertise after careful review of the results of data published in scientific journals and conferences. The selection is based on randomized clinical trials that demonstrate significant effectiveness and durability (sustained viral load suppression, increase in CD4 count), as well as good tolerability (low side effects) and dosage. Preferred regimens usually have more data to support them, which is why they're preferred.

Most clinical testing of first-time ARV combos involves three possibilities:

- 2 NRTIs + 1 NNRTI
- 2 NRTIs + 1-2 PIs
- 3 NRTIs

### Triple nukes

Triple NRTI combos are no longer recommended as first-time combos because they're not strong enough against HIV. But they may be used after another treatment combo has decreased viral load to undetectable levels. Therapies combining four drugs cause more side effects without evidence that they're more effective.

### Combos with non-nukes

A combo that contains one NNRTI is often chosen as a first-time ARV treatment because it's easy to use, reduces viral load, has fewer side effects and interacts with few other drugs. At the moment, clinical trial outcomes favour efavirenz (Sustiva<sup>®</sup>) (except for women who are trying to become pregnant), and



**First-time  
combos**  
Your tear-out  
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nevirapine (Viramune®) is another good option — except for women with a CD4 count higher than 250 cells/mL and men with a CD4 count higher than 400 cells/mL, because of an increased risk of allergies.

## PI combos

First-time PI combos usually include a small dose of ritonavir that boosts the levels of many other drugs by slowing down the rate at which the liver eliminates them. This makes for higher, more effective levels without having to increase the oral dose — allowing it to be more potent. Because lopinavir/ritonavir has very few cases of documented resistance, more research has been done on this combo than any other recommended, ritonavir-boosted PI combo (atazanavir/ritonavir, indinavir/ritonavir, or saquinavir/ritonavir). However, atazanavir is less likely to disrupt lipid levels (cholesterol and triglycerides).

## Nuke combos










Two NRTIs make up the backbone of any first-time combo. Zidovudine with lamivudine or tenofovir with lamivudine or emtricitabine (which is not yet available in Canada) are the top two recommended choices. A stavudine-zidovudine combination is not recommended because they cancel each other out, nor are combos involving stavudine and zalcitabine because of more frequent side effects. Stavudine and didanosine should be used with caution for the same reason.

## Conclusion


An effective drug combo that factors in your lifestyle, dosage, side effects, co-existing health problems (hepatitis, diabetes, high blood pressure, hypercholesterolemia, etc.) and interactions with other drugs will definitely be more successful in lowering your viral load to an undetectable level and restoring your immune system. Take your time in making this very important decision and be sure to use all your resources.

Many AIDS Service Organizations and community groups (listed on pages 8-9) can provide you with valuable information and first-hand advice, as can your nurse and pharmacist. Consider your options and your doctor's advice and choose a combo that's right for you. **R**

## Protease inhibitors (PIs)

PI	Dosage	Possible side effects
 Amprenavir (Agenerase™)	8 pills twice a day <i>or</i> 8 pills + 2 RTV daily <i>or</i> 4 pills + 1 RTV twice a day <i>Take with food</i>	Rash, diarrhea, nausea, ↑ lipids, ↑ glucose, ↑ liver enzymes, fat redistribution
 Atazanavir (Reyataz™)	2 pills daily <i>or</i> 2 pills + 1 RTV daily <i>Take with food</i>	Diarrhea, nausea, jaundice
 Fosamprenavir (Telzir™)	2 pills + 2 RTV daily <i>or</i> 1 pill + 1 RTV twice a day <i>or</i> 2 pills twice a day fat redistribution	Rash, diarrhea, nausea, headaches, ↑ lipids, ↑ glucose, ↑ liver enzymes,
 Indinavir (Crixivan®)	2 pills three times a day <i>or</i> 2 pills + 1 RTV twice a day <i>Fasting state, or take with a light snack</i> <i>Drink a lot of water (2 litres daily)</i>	Kidney stones, low blood sugar, ↑ triglycerides, nausea, fat redistribution
 Lopinavir/ritonavir (Kaletra®)	3 pills twice a day <i>Take with food</i>	Diarrhea, nausea, ↑ triglycerides, low blood sugar, fat redistribution
 Nelfinavir (Viracept®)	5 pills twice a day <i>or</i> 2 pills twice a day	Diarrhea, fat redistribution
 Ritonavir RTV (Norvir®)	6 pills twice a day Also available in liquid formula <i>Take with food.</i> <i>Keep refrigerated until you open the bottle.</i>	Nausea, diarrhea, abnormal sensations in the mouth, hepatitis, loss of strength and/or energy, ↑ triglycerides
 Saquinavir (Fortovase®)	6 pills three times a day <i>or</i> 2 pills + 4 RTV twice a day <i>or</i> 8 pills + 1 RTV daily <i>or</i> 5 pills + 1 RTV twice a day <i>Take with high fat meal</i>	Abdominal bloating, ↑ lipids, ↑ glucose, ↑ liver enzymes, fat redistribution
 Saquinavir SQV (Invirase®)	2 pills + 4 RTV twice a day <i>or</i> 8 pills + 1 RTV daily <i>or</i> 5 pills + 1 RTV twice a day <i>Take with high fat meal</i>	Diarrhea, nausea, ↑ lipids, ↑ glucose, ↑ liver enzymes, fat redistribution

## Fusion inhibitors

Fusion inhibitor	Dosage	Possible side effects
 Enfuvirtide T-20 (Fuzeon®)	One subcutaneous injection twice a day	Skin reaction around area of injection (irritation, swelling, nodule formation), pneumonia and hypersensitivity reaction

Special thanks to Dr. J. Antony Gagnon and Rachel Therrien for drug photos. From: [www.hivmedicationguide.com](http://www.hivmedicationguide.com)

## First-time combos\*

Preferred combos	ARVs	Number of pills
1 NNRTI + 2 NRTIs	→ efavirenz (Sustiva®) + → lamivudine (3TC <sup>-</sup> ) <i>or</i> emtricitabine** + → zidovudine (AZT) <i>or</i> tenofovir (Viread®)	2-3
1-2 PIs + 2 NRTIs	→ lopinavir/ritonavir (Kaletra®) + → lamivudine (3TC <sup>-</sup> ) <i>or</i> emtricitabine** + → zidovudine (AZT)	8-9

\* As per US Department of Health and Human Services (DHHS) guidelines, October 2004

\*\* Not yet available in Canada