Strategies for starting HIV treatment

Deciding when to start treatment and what to use can leave many people feeling overwhelmed. Taking treatment can greatly slow the course of your HIV disease, extend your life and improve your quality of life. It may also cause side effects. You have time to get informed about your HIV disease as well as about when to start and what to start. This publication can help you do that.

There’s no definitive answer on the best time to start. Some people choose to put off taking meds for as long as safely possible. Others decide to start earlier in the course of their disease. Both strategies have merit and both are supported by some research. Whatever your strategy, your willingness to commit to taking therapy over the long-term as well as getting informed up front on all your options can influence how well you do.

Charting out your second and perhaps third regimen ahead of time can be extremely helpful. For instance, you may start one regimen, but then find that the drugs don’t work as well as you hoped. You can then proceed to the second with more confidence rather than being overwhelmed because your first choice didn’t quite work out.

When to start therapy

It’s possible to start HIV drugs at any point in the course of your HIV disease. This is true even if you didn’t find out you have HIV until you became ill. It’s never too late to start and benefit from therapy, although starting earlier rather than waiting too long may decrease damage to the immune system, promote better long-term health outcomes, and further extend your life.

To help guide people with their treatment decisions, a group of researchers, doctors, people living with HIV, and their advocates regularly meet to discuss the results of studies and their experiences treating and living with HIV. This group is called the Federal Guidelines Panel, and every year or so they update the US “Guidelines.” The excerpts below are for adults and adolescents. The complete Guidelines can be found at www.aidsinfo.nih.gov/guidelines.

These Guidelines are meant to help guide people through the issues that may arise while using therapy, including when and what to start. They’re not absolute rules. When enough information is known about some aspect of treating HIV disease, the Guidelines will recommend or suggest a preference. When data are less clear, they will state just that.

What will help further guide decisions around when to start are the results from the START study, which just began enrolling in 2010. However, the full results likely won’t be available until 2014. Project Inform also has a position paper on when to start, available at www.projectinform.org/when.
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Some questions to answer before starting your first regimen ...

What is your current CD4 count?
- Overall, what is the trend? Increasing? Decreasing? Stable?
- Is it above 500, below 200, or in between?
- Are you aware of the health risks related to a count below 200?

What is your current viral load?
- Overall, what is the trend? Increasing? Decreasing? Stable?
- Is it below 10,000? Undetectable?
- Is it above 55,000 or steadily climbing on two or more tests?

Are you aware of the possible side effects?
- Do you know what side effects may give you the most problems, like nausea or diarrhea?
- Are you aware which may happen only within the first week or so and are likely to get better over time?
- Are you aware of the signs of more dangerous or long-term side effects? Do you have another regimen to switch to?
- Do you know what you can do to help avoid or lessen them? (Read Project Inform’s publication, Dealing with Drug Side Effects.)

Are you ready and willing to commit to therapy?
- Do you feel confident that starting now is right for you? What makes you feel this way?
- Have you taken medicine that you had to take on time every day? Was that easy or difficult?
- Are you anxious or worried? Have you talked with your doctor about your concerns?
- What situations might make you miss a dose?
- Do you want privacy and in what situations?
- Where’s best place to store your meds so you can get to it and not forget to take it?
- Does your doctor’s office, clinic or local AIDS organization offer services to help you take your meds as prescribed?

Do you know which therapies may preserve more options for later?
- Have you considered what your second, and perhaps third, regimen will be if your first doesn’t work?
- Have you read about the drugs that are being studied and how they may be used?
- Do you want to start with the most potent combination, or would you rather save those drugs for later?

Are you aware of how therapy may impact your life?
- How do you feel about taking pills every day, perhaps for the rest of your life?
- In the first days or weeks after you start therapy, what support and flexibility do you have with commitments like work, taking care of children or volunteering?
- Will starting treatment limit you taking part in activities that you enjoy?
- How do you plan to carry your meds with you? If you’re away from home overnight? Or on vacation?
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### basic federal guidelines for when to start therapy

Updated January 2011

- HIV treatment is recommended started in anyone with CD4 counts below 500. Everyone below 350 should be on treatment.
- HIV treatment is recommended regardless of CD4 count for:
  - an AIDS-defining illness
  - certain opportunistic illnesses
  - pregnant women
  - CD4s decline >100 per year
  - viral load >100,000
  - people with HIV kidney disease, called HIVAN
  - hepatitis B virus (HBV) co-infection where treating HBV is warranted
- The risk of death or serious illness in people with CD4s above 350 is low. However, some data — for example the ATHENA study — show that people who start therapy with CD4 counts above 350 will more likely maintain CD4s above 800. A Johns Hopkins study shows that people who started treatment with CD4s below 350 would less likely maintain CD4 counts above 500.
- Starting HIV therapy earlier helps reduce the transmission of HIV.
- Factors weighing against early treatment are:
  - lifelong treatment;
  - lack of long-term data on the newest HIV drugs;
  - potential for developing drug resistance; and
  - interference with quality of life.

### the best starting combination

What is the best combination for people starting therapy?

The question of what combination of HIV drugs a person should use as first line therapy can appear confusing. However, there are a few factors to consider which narrow the range of choices for first line therapy. They include:

- its potency
- its ease of use: how many pills and how often
- its potential for short- and long-term side effects

The Guidelines recommend certain regimens as first line therapy, and also give alternative options to these preferred regimens. Consult the chart on page 4.

### Remember the goals of therapy ...

Being on effective HIV drugs should increase your CD4 count and lower your HIV level as low as possible, preferably to undetectable below 50 copies. This should happen without causing severe side effects or harming your quality of life. The regimen should be easy enough to take so you can take every dose as prescribed (adhere well).

Adhering to medicines cannot be stressed enough. The most common reason for failed therapy is missed doses. So, adherence must play a significant role in the decisions you make about treatment. Project Inform’s publication, *Adherence: Keeping up with Your Meds*, can help you prepare for and maintain good adherence.

Five classes of HIV drugs are approved:

- NRTIs/NtRTIs (*nucleoside/nucleotide reverse transcriptase inhibitors*)
- NNRTIs (non-nucleoside reverse transcriptase inhibitors)
- PIs (protease inhibitors)
- Entry inhibitors
- INIs (integrase inhibitors)

Each class works in different ways to stop HIV from making more of itself, called replication. Currently, three or more HIV drugs together forms an effective regimen. For first line therapy this usually includes two NRTIs and either one NNRTI, PI or INI. A list of these drugs can be found in the Drug ID Chart on page 4.
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Two common tests for checking immune health

Throughout your HIV disease, you will get two blood tests done often. This first is a CD4 count (the higher the better), which is the number of an important type of immune cell. The second is your viral load (the lower the better), which is the amount of HIV found in a sample of your blood. Taken together with other blood tests, these results give you a better picture of your general health and immune system.

It's important to be specific and reasonable about your goals in terms of lower HIV levels and higher CD4 counts. One goal could be to raise CD4s by 30% within a year. Another goal could be to lower viral load to undetectable within the first six months, or even the first few weeks. Just keep in mind, the higher your viral load before starting therapy, the longer it may take to suppress your HIV infection.

For more information on these tests, read Project Inform’s publication, Blood work: Two common tests to use for monitoring HIV disease.

federal recommendations for first line therapy (jan. 2011)

<table>
<thead>
<tr>
<th>TRADE NAME</th>
<th>GENERIC NAME</th>
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<tbody>
<tr>
<td>NNRTI-based:</td>
<td>Atripla (1x/day)</td>
</tr>
<tr>
<td>PI-based:</td>
<td>Prezista/r + Truvada (all 1x/day)</td>
</tr>
<tr>
<td>INI-based:</td>
<td>Isentress (2x/day) + Truvada (1x/day)</td>
</tr>
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<td>Pregnancy:</td>
<td>Kaletra + Combivir (all 2x/day)</td>
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<tr>
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<td>DAILY</td>
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<tr>
<td></td>
<td>Invirase/r (2x/day) + Truvada</td>
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</table>
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NRTIs and NtRTIs

NRTIs and NtRTIs are almost always used as part of an HIV regimen. Usually two are taken with a drug from another class. Although there are many drugs in this class, only a few are considered for first line therapy. (Check the Drug ID Chart.)

The Guidelines recommend the combination pill Truvada be used in first line therapy. This has two HIV drugs in one pill. The combo pill Epzicon is listed as an alternative because of a potential serious rash that can occur with using Ziagen drug in the pill. The combo pill Combivir is also listed as an alternative, mainly because the Retrovir in it causes more loss of fat in the face than other first line NRTIs.

The Viread in Truvada has been linked with kidney problems and bone loss. Each of these side effects is uncommon but they can be serious when they do occur. People with pre-existing kidney problems or bone loss should weigh the pros and cons.

The Ziagen in Epzicon can cause a serious allergic reaction called hypersensitivity reaction. A blood test — called an HLA test — can predict whether a person is at risk. Anyone considering Ziagen, Epzicon or Trizivir should get the HLA test done first. Ziagen may also increase the risk of heart attacks, as described in several studies. However, other studies have not confirmed this.

For people with hepatitis B (HBV), three of the NRTIs are also active against HBV: Viread, Epivir and Emtriva. It’s important to know whether or not you have HBV before starting HIV therapy because the doses of these drugs may need to be changed.

A couple of older NRTIs are not routinely used in first line therapy: Zerit and Videx. Zerit is considered inferior and Videx can be difficult to take because of its dosing. NRTI combinations that should not be used include Zerit + Videx, Zerit + Retrovir, Emtriva + Epivir or Viread + Ziagen.

NNRTIs

NNRTIs work differently than NRTIs, but at the same place in its replication cycle. There are four in this class: Intelen, Sustiva, Viramune and Rescriptor. Because of serious side effects, a person would never use two or more NNRTIs at a time.

In first line therapy, one NNRTI is regularly used with two NRTIs. Regimens with Sustiva have been compared to other regimens and have consistently proven both potent and long-lasting. Sustiva is listed in the Guidelines as a preferred first line drug.

Even though the Guidelines recommend Sustiva, Viramune may also be used at times. This is mainly true for people who wish to save PIs for later, but who are concerned about the brain-related side effects of Sustiva. These may include vivid and disturbing dreams, difficulty concentrating, insomnia and mood changes. In studies, 14–53% of people reported these side effects. Most doctors report higher rates of these side effects in their patients.

Viramune is listed as an alternative, mostly due to its risk of serious liver toxicity. This happens mostly in people who start it at higher CD4 counts. It should not be started in women with CD4s above 250 or in men with CD4s above 400.

The risk for rashes from Viramune appears to be slightly higher in women than men. In these women, it’s more likely to be severe. However, pregnant women and women trying to get pregnant should avoid Sustiva at least in their first trimester. If their CD4 counts are below 250, they may consider Viramune a better option when starting a regimen without a protease inhibitor.

Intelen has not been well studied in people taking HIV drugs for the first time and should not be used without signs of current resistance.

The newest NNRTI, Edurant, is only approved for people new to treatment and with viral loads below 100,000.

Sustiva, Viramune and Rescriptor are highly cross resistant. This means that when HIV becomes resistant to one of them, it will likely be resistant to the others, making them less useful. Of the four NNRTIs, Rescriptor is used the least because of its dosing and drug interactions.
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Protease inhibitors
This class of drugs contains some of the most potent HIV drugs available. Factors to consider when using them for first line therapy include their ease of use and possible long-term side effects. Some doctors prefer to save PIs if or when other less complicated regimens have failed. Although this may be an excellent strategy, not enough studies have yet been done to prove this is the best choice.

As a class, PIs tend to affect blood fats, some more so than others. This means that over time your cholesterol and triglyceride levels may increase. People who already have heart disease before starting therapy may want to save PIs for their second or third regimen.

There are a wide range of options for first line therapy. The preferred PIs are potent and generally well tolerated for people on first line therapy. The alternative PIs should work well for most people taking their first regimen, but the research is either not as extensive or as favorable as for those listed as preferred. The preferred and alternative options include Prezista, Reyataz, Kaletra, Lexiva or Invirase. Check the chart on page 4 for the actual regimens.

Entry inhibitors
There are two entry inhibitors in use today: Fuzeon and Selzentry. Fuzeon hasn’t been studied in first line therapy mostly because it’s given as a shot twice a day, which is challenging for people starting their first regimens. Selzentry has been studied in first line therapy, but it failed to match up to the potency of Sustiva. However, in some cases it may be used in first line therapy, though it’s not as strong as a recommendation as the preferred regimens.

Integrase inhibitors
Integrase inhibitors are the newest class, and Isentress is currently the only one. As such we don’t know enough about its long-term side effects, although it’s generally well tolerated and is proving to be a potent HIV drug. Isentress is a recommended preferred option for first line therapy.

What to start first: NNRTIs or PIs?
No large study has yet been done that definitively shows which drug class is the better to start. So far, we know that when a person’s HIV level remains under 50 (undetectable) for at least one year on therapy, it usually remains that way for at least another two years, assuming good adherence. This is true for almost any regimen used.

It’s less clear how much the choice of a first regimen impacts how well a second one will work. In most cases if a person starts therapy with a PI, he or she will likely be able to use Sustiva successfully as second line therapy. So far, there are less data the other way around, but there’s no reason to think it would be any different.

Perhaps the most limiting factor of all the drugs is cross resistance. When a person’s HIV develops a high level of resistance to one drug in a class, it will generally have at least some resistance to many of the other drugs in that class. When HIV develops even low levels of resistance, it causes the drug to be less potent.

Some people believe that the best first line strategy is to take whatever is the most potent. The most powerful and long-lasting effects come from a person’s first regimen. The longer a person stays on it without major side effects or resistance, the better. As a rule, boosted PIs like Prezista and Kaletra are considered the most potent and long-lasting.

Others feel that saving potent and longer lasting medications for second line therapy is the better strategy, and that starting treatment with an NNRTI is better. This would likely work for most people for some time, and it keeps PIs for later. Unlike the PIs, it’s also hoped that the NNRTIs and NRTIs will have fewer long-term effects on cholesterol and triglycerides or changes in fat, though these data are mixed. Again, the theory has some merit, but no studies prove this is the better long-term strategy.
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Starting therapy in women
For the most part, the recommendations for when and what to start are the same for women and men. If a woman is not pregnant, not planning to become pregnant and not taking hormonal contraceptives, by and large their treatment recommendations are the same as for men. While HIV drugs have not been studied as extensively in women, most evidence to date shows that they work as well for both.

The Guidelines recommend that all HIV-positive pregnant women be on HIV therapy, regardless of their CD4 counts or HIV levels. Some doctors recommend that they wait to begin treatment until their second trimesters (13–24 weeks). Since the first trimester is when the baby’s major organs develop, this is when birth defects from taking medicines will most likely occur. Some HIV drugs should NOT be taken during pregnancy: Viramune in women with CD4s above 250, Zerit + Retrovir which can cause serious side effects, and Sustiva which can cause birth defects.

Some HIV drugs interact with oral contraceptives or other female hormone replacement therapies. So it may be necessary to adjust the dose of the oral contraceptive, use other methods of birth control, or change your HIV drugs.

HIV drug resistance testing
Data show that up to 1 in 6 of all newly infected people in the US have drug-resistant strains of HIV. About 5% of these are resistant to more than one class of drugs. For this reason, it’s recommended that people get resistance testing done before choosing their first regimen, best done when viral loads are above 1,000. For more information, read Project Inform’s publication, HIV Drug Resistance and Resistance Tests.

In conclusion
Project Inform believes that HIV treatment decisions should be driven by a combination of the best available medical data, a person’s unique life situation, medical history and personal preference. We also recognize that in most diseases earlier treatment usually leads to better treatment outcomes. There’s no evidence to suggest this would not be true for HIV disease.

Your doctor may have strong opinions about when to start therapy or which regimen is best for you. Your opinion and concerns count too. Share them with your doctor(s) so they can help you build the best strategy for you. Project Inform’s publication, Building a Cooperative Patient / Doctor Relationship, offers tips.

Because it’s your life and your body, only you can ultimately decide how you wish to balance the need to keep your HIV in control with any risks for disease progression and side effects. With over two dozen HIV drugs on the market today — many of which are simpler to take and seem to have fewer short- and long-term side effects — you can probably find a regimen that works best for you.

Remember to ask a lot of questions: of yourself, your doctor, other people living with HIV, and information sources like Project Inform. Plot out your strategy so it includes other aspects of general health maintenance and possible second or third line options. Take your time, be prepared and then enjoy your life to the fullest degree possible, knowing you’ve made the best decision you could have.

Things that might help to ask your doctor
• What if I’m not ready to start therapy?
• What regimen(s) do you recommend and why? Is one better than another?
• What is my next regimen if the first one doesn’t work?
• How do my CD4 count and HIV level affect my decision to start?
• What are the possible side effects of the drugs I would take?
• How many pills would I take? How often? With or without food?
• When should I let you know if I think something is wrong?
• What do you mean when you say I should adhere to my drug regimen?
• Are there are any other tests that I should take before starting a regimen?
Filling this out before your next doctor’s appointment can improve your discussions about starting HIV therapy.

What factors do you consider most important in selecting your first regimen?

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<thead>
<tr>
<th>Factor</th>
<th>MOST IMPORTANT</th>
<th>VERY IMPORTANT</th>
<th>LESS IMPORTANT</th>
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<tr>
<td>Long lasting</td>
<td>4</td>
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<tr>
<td>Fewer pills in each dose</td>
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<td>Dosing only once or twice a day</td>
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<td>Low chance of stomach side effects</td>
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<td>Low chance of brain-related side effects</td>
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<td>3</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

After looking over the available information on HIV therapies, what are two possible combinations that appear to meet the most of your concerns?

Regimen #1: 
Regimen #2: 

My reasons for considering these regimens:

Concerns I have about these regimens:

Side effects to discuss with my doctor and plan for:

Adherence strategies I will use include:

Questions to ask my doctor: