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November 2007

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Introduction to Combination Therapy

First questions

You and your doctor

Adherence

Resistance

Which combinations

HIV i-Base publications:
Guide to Changing Treatment
Guide To Avoiding and Managing Side Effects
HIV, Pregnancy and Women's Health
Guide to HIV and Hepatitis Coinfection
HIV Treatment Bulletin
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If you have questions after reading this guide, i-Base runs a free treatment information phonenumber for information and support on all aspects of HIV treatment.

0808 800 6013

**Monday, Tuesday and Wednesday
12-4 pm**

Calls are free from UK landlines and Orange network. If calling from outside the UK, please call +44 20 7407 8488

The website also has a question and answer service where questions can be answered online and by email:

www.i-base.info/questions

Disclaimer: Decisions relating to your treatment should always be taken in consultation with your doctor. Information in this booklet is intended to support those discussions.

Introduction

Information about HIV treatment can change quickly, so make sure any information you read is up to date. Be careful of information, whether printed or from the internet, that is not clearly dated.

We have updated this guide at least every year for the last eight years. If you are reading this after November 2008, please call i-Base for a new edition.

References are to current UK, European and US treatment guidelines. These documents including useful tables.

www.bhiva.org

www.eacs.eu

www.aidsinfo.nih.gov

Changes to this edition include:

- A new format smaller booklet with a few more pages.
- A stronger caution against treatment interruptions, based on results from the SMART study.
- A discussion on starting treatment at CD4 counts between 200 and 350.
- * The section on choosing drugs and combinations has been rewritten to focus on the most frequently used drugs.
- * References to new drugs have been updated, including Atripla, darunavir, raltegravir and maraviroc.
- New pages to record important details about your treatment history, including results from blood tests and treatment choices.

First questions: what, when, why and other questions...

What is combination therapy?

Combination therapy is the term for using three or more drugs to treat HIV. It is also called triple or quadruple therapy or HAART (Highly Active Anti-Retroviral Therapy). HIV drugs are also called ARVs.

There are now at least five different types of drugs that work at different stages of the HIV life cycle. (See Figure 1).

Do the drugs really work?

In every country that uses ARVs, there has been a dramatic drop in AIDS-related deaths and illnesses.

Treatment works for women, men and children. It works no matter how you were infected with HIV. Whether this was sexually, through IV drug use, or by blood or blood products.

Taking HIV drugs, exactly as prescribed, will reduce the virus in your body to tiny amounts - but it does not get rid of the virus.

This then lets your immune system recover and get stronger by itself.

How to check treatment is working

Regular monitoring, using blood tests, will check that the drugs continue to work.

- Viral load tests measure the amount of HIV in your blood. Results are given as copies/mL.
- CD4 tests measure your immune system. Results are given as cells/mm³.

Even if you start with a very low CD4 count, you could regain enough of your own immune system for your body to recover from many HIV-related illnesses.

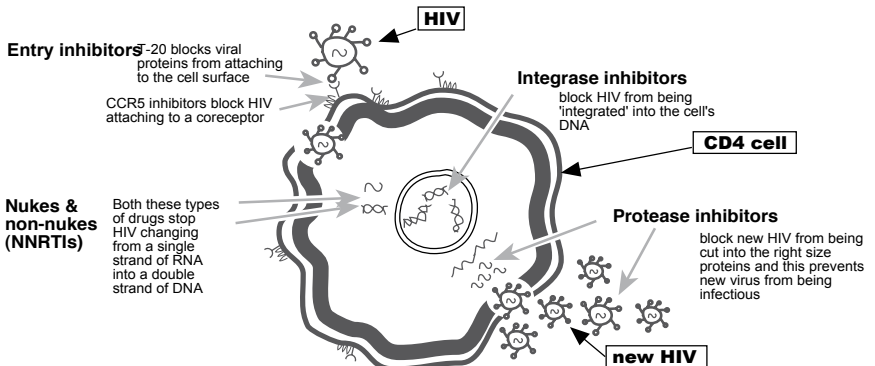
If you use HIV treatment at the right time, and in the right way, you will stay well much longer.

How do the drugs work?

HIV drugs work by stopping the virus from making copies of itself.

Fig 1: HIV lifecycle - how drugs work in different ways

Each CD4 cell is used to produce hundreds of copies of HIV.
Different drugs block different parts of the HIV lifecycle.



Even if you are well now, it's a good idea to get to know something about treatment before you need it

This brings viral load down to tiny levels and your immune system (CD4 count) then has a chance to become stronger again.

How long will the drugs work?

Combination therapy using at least three drugs has now been used for over ten years. Many of the individual drugs have been studied for even longer.

How long a combination will work depends on not developing resistance. This in turn depends on getting, and keeping, your viral load to undetectable levels, below 50 copies/mL.

If your viral load stays undetectable, you can use the same combination for many years.

In UK guidelines, getting your viral load below 50 is a main goal of treatment.

Does everyone need treatment?

At some point, most HIV-positive people will need treatment. When people will need it though, varies from person to person. HIV infection progresses in different people at very different rates.

- About one third of HIV-positive people will stay well for up to 10 years after infection, even without treatment.
- 60% will start treatment after 4-5 years.
- 2-3% of people can become ill more quickly and need treatment much earlier.
- 2-3% of people can go for 15-20 years without treatment.

Whether you need treatment is something you have to discuss with your doctor. This will usually take place over several visits.

When discussing treatment:

- Ask as many questions as possible until you are happy with the answers.
- Get useful information from other sources. This includes the internet, friends, newsletters and phonelines.

Even if you are well, it is a good idea to get to know something about treatment now, before you need it.

This is particularly important if your CD4 count is falling, or if you have a high viral load.

When should I start treatment?

When to start treatment is something you and your doctor must discuss together. You are the person who has to take the pills. So, you have the choice over whether you start, as well as which drugs you use.

UK current guidelines recommend starting treatment before your CD4 count falls below 200 cells/mm³. The next UK guidelines will probably recommend starting between 200 and 350 based on recent studies that show there are benefits to earlier treatment.

They also recommend that a patient needs to be ready for treatment. This is important. Even at a count of 200, you do not need to start treatment straight away if you are not ready.

- Ask about the different drugs that you can use. You need to know the good and bad things about each of them.
- Take time to think about what you want to do. Do not feel rushed or pressurised into doing something you don't understand.

- If you have only recently been diagnosed, you are likely to need time to come to terms with this before you are ready to start treatment.

CD4 count and risk of becoming ill

Your CD4 count is the most important test for deciding your risk of becoming ill. How fast it is changing is also used to decide when to start treatment.

While your CD4 count is above 300, you still have a good immune system. Below 300, you are at a higher risk of infections that cause diarrhoea and weight loss.

If your CD4 count falls below 200, your risk of developing a pneumonia called PCP increases. Below 100, your risk of serious illnesses increases even further.

A low CD4 count does not mean that you will definitely become ill. It is just more likely. Most drugs used to treat these HIV-related illnesses are much more difficult to take than anti-HIV drugs.

Although you may be worried about using treatments, HIV and AIDS is still a very real and life-threatening illness. You can delay treatment until it is too late! Illnesses that can occur at any time when your CD4 count is below 200 can be fatal.

How are viral load results used?

Although viral load results can also be used to decide when to start treatment they are more important after you start treatment.

When viral load falls it shows the drugs are starting to work.

Once viral load is undetectable, it shows the drugs continue to work. If it goes up it shows the drugs may not be working.

Are recommendations the same for men and women?

There are some differences between HIV in women and men. One of these is that at the same CD4 count, women can have a slightly lower viral load than men. Some studies also show that women have a higher risk of becoming ill than men at the same CD4 count. This may be a reason for women to start treatment earlier than men. The evidence to support this was not strong enough for this to be included in treatment guidelines.

An American study found that viral load levels vary during the different stages of the menstrual cycle. It may be a good idea, for you and your doctor, to make a note of where you are in your cycle when you have these tests. You can then make an allowance for this when you get the results.

What about treatment in pregnancy?

HIV can be treated very safely and effectively during pregnancy.

In addition, treatment with combination therapy that reduces viral load to below detection dramatically reduces the risk of transmitting HIV to your baby to almost zero.

Women who start treatment with a CD4 count that is above 250 cells/mm³ should not use the drug nevirapine because they are at a higher risk of liver toxicity. This caution also applies to pregnant women.

Treatment during pregnancy is a specialised area. For more information see the i-Base guide '**HIV, Pregnancy and Women's Health**'.

How do children use HIV treatment?

The principles for treating children with HIV are very similar to those for treating adults. But, there are some important differences.

The immune system and drug absorption can be different in babies, toddlers, infants, children, adolescents and adults. This is why specialist paediatric HIV care is recommended at all ages.

CD4 counts are higher in children than adults. A new-born baby, for example, can have a CD4 count that is 2-3000 cells/mm³.

Because of this, children are monitored using CD4 percentage (CD4%). This is the percentage of white blood cells (lymphocytes) that are CD4 cells. The CD4% of an HIV-negative person is around 40%. A guide to children's CD4 count and CD4% by age is included in Table 1.

Table 1: CD4 count and equivalent CD4% for babies and children by HIV disease category

Age HIV stage	less than 12 months	1-5 years	6-12 years
Category 1 (no damage)	over 1500	over 1000	over 500
	over 25%	over 25%	over 25%
Category 2 (moderate)	750-1500	500-1000	200-500
	15-24%	15-24%	15-24%
Category 3 (severe)	less than 750	less than 500	less than 200
	less than 15%	less than 15%	less than 15%

There are separate treatment guidelines for children. However, they tend to be updated less frequently than adult guidelines. It is therefore important to be aware of changes in adult care that may be just as relevant for children.

For more information about children and HIV, visit the Children with HIV Association (CHIVA) and PENTA websites:
www.chiva.org.uk
www.penta.org

Is age an important factor in adults?

Combination therapy may reactivate an important part of your immune system called the thymus. Previously, most doctors thought it stopped working in adolescence.

The thymus may become active again in people in their 30s who are HIV-positive and using combination therapy. This finding isn't yet fully understood. It may mean that there are advantages to starting treatment when in your 20s or 30s.

Ageing suppresses our immune systems and reduces our CD4 count. People over 50 have an increased risk of damage caused by HIV.

The argument for starting treatment probably gets stronger as you get older. Treatment guidelines do not yet comment on this, apart from in reference to heart disease.

Age, HIV drugs and heart disease

Risk factors for heart disease include age (over 45 for men and over 55 for women), sex (male), lack of exercise, family history of heart disease, high blood pressure, smoking and diabetes.

Other risk factors associated with heart disease include raised levels of cholesterol and triglycerides, which can be a side effect of HIV treatment.

Not treating HIV may also be a risk factor. Generally, the benefits of HIV treatment far outweigh any additional risk of heart disease. However, people with higher risk of heart disease should choose their HIV drugs to minimise this risk.

The largest study looking at heart disease and HIV treatment, reported an increased risk of heart disease related to use of protease inhibitor-based regimens, rather than using NNRTI-based combinations.

An assessment of cardiovascular and HIV risk factors is therefore recommended before starting HIV treatment.

Free risk assessment programmes are available on the internet.

UK site with measurements in mmol/L

www.riskscore.org.uk

US site with measurements in mg/dL

hp2010.nhlbihin.net/atpiii/calculator.asp

As with the general population, making lifestyle changes to reduce risk of heart disease is good advice if you are HIV-positive. This becomes more important as the number of other risk factors increases.

Early diagnosis and primary infection

Some people who discover that they are HIV-positive within six months of being infected decide to start treatment straight away. This is regardless of their CD4 and viral load counts.

Using early treatment may enable you to benefit from immune treatments or vaccine-related research in the future. But, you need to balance these potential benefits, against side effects and the risk of resistance. Also, that you may not medically need treatment for many years.

Treatment in primary infection is therefore largely only provided in clinical trials.

If you think that you were infected within the last six months, you can ask for a de-tuned (STARHS) HIV test. This test can confirm a recent infection. Your doctor can access this test free from the Health Protection Agency (HPA) HIV laboratory in Colindale (020 8200 4400).

If you are interested in a trial, you can contact the research unit at St Mary's Hospital (020 7886 6047) or the Royal Free Hospital (020 7472 6232) in London.

Late HIV diagnosis and low CD4s

Some people, across all age ranges, only find out they are HIV-positive when they become ill and are admitted to hospital.

This often means starting treatment straight away, especially when the CD4 count is below 100 cells/mm³.

Even with a very low CD4 count, even below 10 cells/mm³, if you follow your treatment very carefully, you have a good chance that treatment will work. Your viral load will drop and your CD4 count will rise again to safer levels.

This should not be seen as a reason to delay treatment. Starting with a very low CD4 count can sometimes cause dormant infections, such as TB and CMV, to activate. This is called Immune Reconstitution Syndrome.

What about side effects?

Everyone worries about side effects.

But within a few weeks, most people find that taking HIV treatment is easier than they thought. It usually becomes an ordinary and manageable part of daily life.

- Most side effects are usually mild.
- They can often be reduced with other medication that is easy to use or by switching to other drugs.
- There is only a small risk of serious side effects, and these should be picked up by careful routine monitoring.

Ask your doctor, nurse or HIV pharmacist about the most common side effects of the drugs that you want to use. Ask how likely they are to occur. Ask how many people stop treatment because of them (usually very few).

Even rough estimates will give you a good idea of what is involved.

Most common side effects

Nausea (feeling sick), diarrhoea and tiredness are the most common general side effects. These often become easier after the first few weeks. Very rarely, nausea and tiredness can be serious. This is why you should tell your doctor of any problems.

If anti-nausea or diarrhoea medications do not help, ask your clinic for stronger or more effective drugs.

One of the most used drugs (efavirenz) can affect sleep patterns and change your mood. You need information about this before starting treatment. These side effects are usually strongest when you first start treatment.

They usually reduce in most people over the first few weeks. If the side effects continue, you can use another drug.

Lipodystrophy and metabolic changes

Lipodystrophy refers to changes in fat cells and the distribution of body fat. It also refers to changes in blood fat and blood sugar levels (metabolic changes).

We do not know what causes these changes, which usually, but not always, develop slowly over many months.

This is one of the biggest worries for people who are about to start treatment.

Not everyone gets lipodystrophy and new drugs used in first-line therapy do not cause fat loss. The greater awareness of lipodystrophy also means that you will be monitored carefully.

If you have any difficulties, make sure your doctor takes them seriously and does something about it.

Fat loss

Fat loss (from arms, legs, face and buttocks) has only been linked to two drugs - d4T and AZT - which are no longer recommended for first-line therapy.

Fat accumulation

Fat accumulation, to the stomach or breasts and/or across the shoulders or neck, has been linked to combinations that include protease inhibitors and NNRTIs.

Careful body measurements by a dietician, by DEXA scan, or photographs, can monitor changes.

You can change treatment if you get early symptoms. Early symptoms may reverse if

you switch to different HIV drugs. Exercise and dietary changes can also help.

Changes to fat and sugar levels in blood

Most drugs can change fat (cholesterol and triglyceride) and sugar (glucose) levels, which are monitored by routine blood and/or urine tests. These are best performed when you are fasted (ie before you eat or drink anything that day).

Other side effects

More serious side effects can occur with most combinations, although more rarely. They are also linked to specific drugs.

It is important to be aware of these for all the drugs in your combination, before you start treatment.

The i-Base '**Guide to Avoiding and Managing Side Effects**' includes detailed information about side effects:

www.i-base.info/guides

It also contains useful information about how to report side effects to your doctor. For a free copy please call 020 7407 8488.

What is the best combination?

There isn't one answer to this question. This is because drugs that agree with one person can be more difficult to tolerate for another.

Any combination should be:

- Strong enough to reduce your viral load to below detection.
- Be one you can tolerate AND follow the daily schedule AND stick to any dietary restrictions.

The most commonly used combinations are discussed on pages 18-23.

Your doctor will discuss with you which combinations are more likely to get your viral load undetectable. If you have taken HIV drugs before, this will affect how well your next treatment works.

Ask for information about dosing schedules, pill size and side effects. This will help you pick a combination that will be easier to follow.

Can I change treatments?

If your first combination is too difficult to follow, or if any initial side effects have not improved after the first few weeks, you can always change the drug or drugs that are most difficult.

If this is your first combination, you have many choices. You should not put up with difficult side effects for months on end.

Some people use one combination to get their viral load undetectable, and then change to an easier combination afterwards.

What is 'treatment-naive'?

'Treatment-naive' or 'drug-naive' refers to someone who has never used HIV drugs.

Someone who has used drugs before is called 'treatment-experienced'.

Can I take a break in my treatment?

Once you start treatment, taking a break in the future is not recommended, unless you have a serious medical problem with one of the drugs in your treatment.

The largest study to look at treatment interruptions (the SMART study) found an increased risk of both HIV-related and

non-HIV-related illnesses and deaths in people who stopped treatment, compared to people on continuous treatment. This included serious heart, liver or kidney-related disease.

- Stopping treatment for any period is not generally recommended.
- Your viral load can increase again very quickly (from undetectable to several thousand in a few weeks). Each interruption of treatment also carries a risk of developing drug resistance.
- If you want to take a break, it is essential you talk to your doctor first. Some drugs have to be stopped at different times, to reduce the risk of resistance.

Should I enter a trial?

Many hospitals are also research centres and you may be asked to join a trial.

If asked to join a trial, or if you are interested in a trial, take plenty of time to find out about it. Ask for independent advice. Women should ask the percentage of women that are included in the study.

Remember, many combinations that have proven their effectiveness are already available to use. There is no need to join a trial if you do not want to.

However, well-planned studies can offer better monitoring and care than you would normally receive at your regular clinic. This may mean attending your clinic more frequently.

Trials are very important for developing new treatments. They can improve our knowledge of how to use both new and existing drugs.

If you are recently diagnosed, or are only just finding out about treatment, you should not feel pressurised into taking part.

Ask about the alternatives to the treatment proposed in the study. Ask what advantages the study offers over existing treatment.

Your future care will not be affected if you choose not to take part in a trial.

What else do I need to know?

Ongoing research means that ideas about how to use anti-HIV drugs are changing. The treatment your doctor will advise today may be different from 12 months ago.

This isn't just because there are newer drugs available. It is to do with understanding how the drugs work, why they sometimes stop working, and especially increasing knowledge about resistance.

This is why it is important to make sure your information is up-to-date.

Ask questions about anything you don't understand. You can then take responsibility for whatever you decide.

Why do treatments not always work?

For some people the treatments will not work as well.

- The combination may not be potent enough.
- You may already be resistant to one or more of the drugs in your combination.
- Missed or late doses can lead to resistance (even if you are only missing one dose a week).

- One or more of the drugs may not be absorbed properly. There can be big variations between people and tests can check for this.
- Side effects may be too difficult to tolerate.

Trial results never show a 100% success rate. BUT if you have a good doctor, and you follow your regimen carefully, anyone starting treatment for the first time should be able to get an undetectable viral load.

Success rates for people on their second or third therapy are usually lower than for those starting treatments for the first time.

This is often because people continue to make the same mistakes and move to a new combination without understanding why the original one failed.

If you need new drugs in order to put together a new combination, then make sure you and your doctor keep up-to-date on the latest research.

For more information on drug resistance and second-line, see the i-Base '**Guide to Changing Treatment**'.

Are the drugs a cure?

The current drugs are a treatment, but they are not a cure. They stop the progression of HIV. They let your immune system start to repair itself. However, you will still be HIV-positive.

Even people taking combination therapy for many years, with a viral load below 50 copies/mL, still have very small amounts of HIV. This HIV is in cells that are 'resting' or 'sleeping' and is not reached by current drugs.

These sleeping cells are one of the reasons that it is very difficult to find a cure for HIV. Some of these cells can sleep for 70 years.

You may need medication for a long time, but newer drugs may be easier to take and more effective.

This means you may still get to die of old age rather than from HIV.

It may also mean that you are still alive when we find a cure - and this is something good to aim for.

Don't look at the drugs you start with now as a treatment that you will be taking forever. Look at them as something you have to be really committed to for the next couple of years.

Take this new aspect of your life more seriously than anything else until you get it right.

You and your doctor

Developing a good working relationship with your doctor and other healthcare workers, can help your health in the long-term

Nurses and pharmacists are also an excellent source of support and advice on all aspects of your treatment (including adherence and side effects).

They are able to make referrals to other professionals, including dieticians, psychologists and social workers.

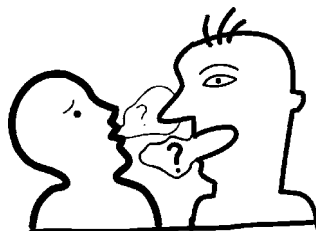
Both you and those involved in your care have certain rights and responsibilities. A list of your rights as a patient and things you can do to help are below.

The following lists include some of your rights and responsibilities as a patient.

Your rights as a patient...

- To be seen within 30 minutes of your appointment. If they are running late, you should expect an explanation.
- To be fully involved in all decisions about your treatment and care.
- To be treated with respect and confidentiality.
- To have different options for treatment explained to you. This should include the risks and benefits of each option.
- For your records to be kept securely. They should be available for you to see if you ask.
- To choose whether to take part in research trials. This will not affect your current and future care.
- To make a complaint about your treatment. Any complaint must be fully investigated. Again, this must not affect your future care.
- To have a second opinion from a suitably qualified doctor.
- If you write to your hospital or clinic, you should have a written response within 14 days.
- To change your doctor or treatment centre without it affecting your future care. You do not have to give a reason for changing doctors or clinics. However, if there has been a misunderstanding, then giving a reason can sometimes help resolve the problem. If you have generally been happy with your treatment, then changing your doctor or clinic should be a last resort.

- To have test results and a summary of your history forwarded to your new doctor or treatment centre.



Things you can do to help...

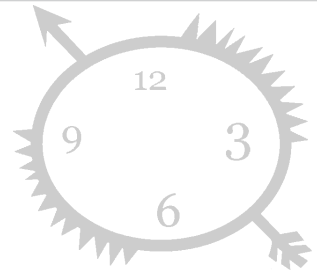
- Find a clinic that is convenient to you and that you feel comfortable with.
- Find a doctor who you like. If you are a woman and want to see a female doctor then ask for this.
- Make a list of things you want to discuss with your doctor. Remember to take it to your appointment!
- Ask to see the same doctor at each visit. This is important. It's difficult to develop a good relationship if you always see a different doctor.
- Have your routine bloods taken 2-3 weeks before your regular clinic visits so the results are ready for your appointment.
- Turn up for your appointments on time. Tell the clinic if you can't make it. Then they can give your slot to another patient.
- Treat all people involved in your care with the same respect you would wish to receive yourself.
- Listen carefully to the health advice that you are given, and act upon it.
- If you don't understand something, ask your doctor to explain it again or in a different way.
- Be honest with those caring for you. Tell them about any other drugs that you are taking. This includes legal and illegal drugs or complementary treatment.
- Be honest about your level of adherence. If those managing your care don't know you are having problems, they can't help.

Further advice on your NHS rights are detailed in the department of health booklet **'Your Guide to the NHS'** available by phoning 0800 555777 or online:

nnuh.nhs.uk/docs%5Cleaflets%5C36.pdf

Information about healthcare services including core principles and on how to make a complaint are currently on the 'About the NHS' link on the home page:

www.nhs.uk/



Adherence - and why it is so important

What is adherence?

Adherence is a word to describe taking your drugs exactly as prescribed. This includes taking them at the right time. It also includes following any special diet restrictions.

Good adherence is important to make sure that all the drugs in your combination are present at high enough levels to keep HIV under control, all of the time.

It is important that you develop a routine or daily schedule. You may need some support to get used to the changes treatment makes in your life. Adherence can be very difficult.

This is the most important thing you have to think about when you start taking a new combination.

Start treatment when you can give yourself the extra time and space you may need to adjust.

During the first few weeks, nothing else should take priority over getting your treatment right.

Many treatment centres now have an adherence clinic or an adherence nurse.

How much is enough?

Taking medication exactly on time is very important. However, there is usually a window period of about an hour that is still okay. Some drugs, and some people, have a wider window period than others.

Because of this variation, it is better to aim for the same time each day.

Diet restrictions are very important. Ignoring these can be like only taking half a dose. You will not absorb enough of the drug for it to work properly. Resistance is then more likely to occur.

The next question is: 'exactly how close to perfect adherence do you have to get?'

Unfortunately, the answer is 'almost 100%'... Even missing one or two doses a week, especially when first starting treatment, can have a big impact on a successful result.

- Be strict with yourself in assessing how adherent you are
- If it's not good, you need more support. It is available, but you will need to ask.
- Talk to your doctor, nurse or pharmacist!

Tips to help...

- Choice of treatment. Get all the information on what you will need to do before you start treatment: How many tablets? How big are they? How often do you need to take them? How exact do you have to be with timing? Are there food or storage restrictions? Are there easier choices?
- Plan your timetable (see page 24). For the first few weeks mark off each dose and the time that you took it.
- Contact your hospital or clinic if you have difficulties with side effects. They can prescribe additional medication to help. They can also change the treatment if necessary.
- Use a daily or weekly pillbox. Then you can check if you have missed a dose.

- Use a pill beeper or alarm watch for both morning and evening doses.
- Take extra drugs if you go away for a few days.
- Keep a supply where you may need them in an emergency. This can be in your car, at work or at a friend's house.
- Get friends to help you remember difficult dose times. Ask them to remind you when you are out at night.
- Ask friends what they do and how well they are managing. Most clinics can arrange for you to talk to someone who is already taking the same treatment.
- Ask your doctor for a supply of medications to control nausea and diarrhoea. These side effects are the most common when starting therapy.
- Many combinations are taken once-daily. This usually means taking them every 24 hours. Twice-daily drugs need to be taken every 12 hours.
- Completely missing a once-daily combination may be more serious than forgetting a twice-daily dose. Adherence is especially important with once daily combinations.

What if I forget to take my pills?

Almost everyone will forget or be late with their drugs at some time.

There is a difference though between occasionally missing a dose, and regularly forgetting on a daily or weekly basis.

You need to aim to take all your doses at approximately the right time.

If you are regularly taking them late or missing doses completely, it is important to talk to your doctor about other options.

There may be an easier combination that you can use.

You have to follow your regimen everyday. This includes both during the weekend, and in the different situations involved in life.

Taking days off your regimen is a very dangerous way of using treatment.

There are always things that can help you to avoid missing doses, whatever your lifestyle.

If you realise you have missed a dose, take it as soon as you remember.

BUT, if you only realise when you're going to take your next dose, do not take a double dose.

Recreational drugs and complementary therapy

Some HIV drugs interact with recreational drugs, street drugs, methadone and complementary treatments.

The interactions can be complicated and involve both higher and lower levels of HIV or other drugs.

It is, therefore, very important that your HIV doctor and pharmacist know about any other drugs or supplements that you use.

Even if you use them rarely. Your doctor will treat this information in confidence.

Alcohol does not interact with HIV medications. However, heavy alcohol use, as with recreational drug use, may reduce adherence. It would help if your healthcare workers know about this.

Resistance

What is resistance?

Resistance to drugs occurs when the structure of a virus makes tiny changes that stop the treatment from working. These changes are called mutations.

You cannot develop resistance if you are not taking treatment.

You can be infected with a strain of HIV that is already resistant to some or all HIV drugs.

This is why everyone in the UK should have a resistance test before starting treatment.

You should have a resistance test if you have just been diagnosed with HIV, whether or not you plan to start treatment.

How does resistance occur?

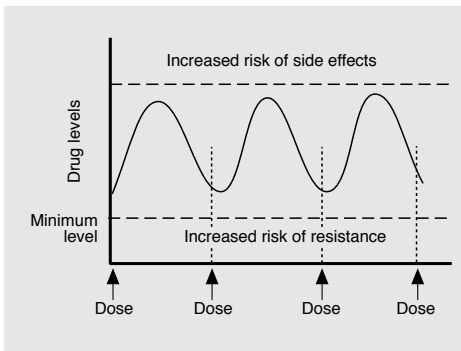
Mutations that lead to drug resistance are generally only produced when you continue taking a treatment when you have a detectable viral load.

If your viral load is still above 500 copies/ml after 2-3 months, or above 50 copies/mL after 6 months, you may need to change your treatment.

Your doctor should look closely at why the results are not as good as they could be. They will want to discuss how you are managing adherence and side effects. They should also test for resistance and possibly drug levels.

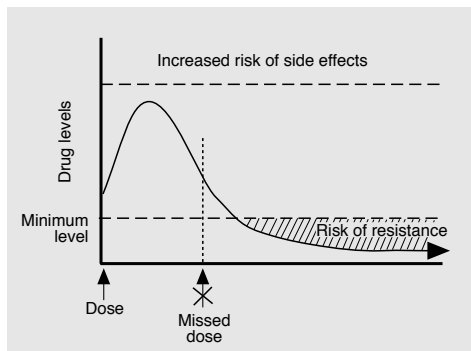
Resistance can develop even at low viral load levels between 50 and 500 copies/mL.

Fig 1: Drug levels with good adherence



Drug doses are calculated so that average drug levels are high enough to be active against HIV without risking resistance - 24 hours a day - and low enough to minimise the risk of side effects.

Fig 2: A missed or late dose increases the risk of resistance



Missing or being late with a drug lets the drug levels fall to a level where resistance can develop.

The more often you are late or miss a dose, the greater the chance this will occur.

What do the letters and numbers in resistance test results mean?

Resistance mutations are usually given a number to say where on the viral DNA that the change has taken place - like junction numbers on a motorway.

If there is a letter afterwards, this stands for the new chemical that the mutation makes. If there is a letter before this stands for the chemical that has been changed.

You should have a viral load test four weeks after starting or changing treatment. This should then be checked every 3 months when on treatment.

Get the results when they are ready (usually after two weeks). Don't just wait until your next visit.

Some clinics let you get your blood tested 2-3 weeks before you see your doctor. Then you will have the results back for the appointment.

If your viral load has increased, you should then get a second test on the same day, to confirm the results.

Often slight increases are due to errors in the test. You can also have small increases that go back down again that are called 'blips' or 'spikes'.

A re-test will check what is happening. If the combination is failing, you minimise the risk of further resistance by checking this straight away.

You will get a better response to a second

treatment if you change when viral load levels are still low.

How do I avoid resistance?

You need to use a combination that is strong enough to control the virus, and you need to take it on time, every day.

In treatment guidelines, avoiding resistance is more important than an increase in your CD4 count. Avoiding resistance will let your treatment work long-term.

If you get your viral load to under 50 copies/mL, you dramatically reduce the risk of resistance. If you are starting treatment, this is a realistic goal.

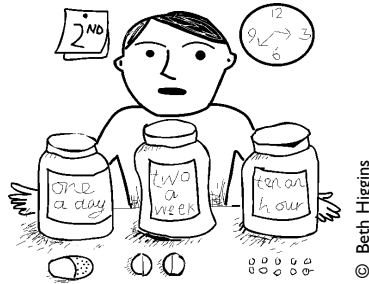
What is cross-resistance?

Cross-resistance is when resistance to one drug causes resistance to other similar drugs, even if you have never taken them before. This is particularly true of drugs in the same class.

Fig 2 -The importance of different viral load levels when on treatment

less than 50 (<50 copies/mL)	So little HIV is produced that resistance is unlikely to develop to your combination. So long as you continue taking the drugs carefully, you could use them for many years.
between 50–500 (>50 and < 500 copies/mL)	This is not low enough to stop resistance. At some point, as resistance becomes more extensive, the drugs will stop working and your viral load will rebound much higher.
over 500 (>500 copies/mL)	If you continue to take treatment while your viral load is detectable (and not still falling) resistance will mean you can only use your combination for a limited time.

Which drugs, which combination?



Even though there are over 20 HIV drugs and hundreds of potential choices, only two main types of combination are recommended.

Guidelines recommend starting with either:

2 nukes + an NNRTI
or
2 nukes + a ritonavir-boosted PI

Within each class, only a few drugs or combinations are recommended.

Knowing about other options is important in case you have trouble with these main options.

First combination

The first combination offered in the UK usually includes:

efavirenz (an NNRTI) + *EITHER*
Truvada (tenofovir+FTC) *OR*
Kivexa (abacavir+3TC)

This is because efavirenz is one of the best drugs at bringing down viral load and it is one pill, once-daily. Even though side effects are not straight-forward, the risk of serious side effects is low.

If you don't want to use efavirenz because of the type of side effects it causes or

because you want to become pregnant, then the current choice is to use **EITHER** another NNRTI (nevirapine) **OR** a boosted PI. Information about these drugs is included on page 20.

Starting on efavirenz

Since 2005, UK guidelines recommended the NNRTI **efavirenz** as first choice because it a potent, once-daily drug with a lower risk of serious side effects.

However, the main side effects of efavirenz relate to the Central Nervous System (CNS). This can include mood changes such as anxiety, euphoria and depression; and sleep disturbance that includes vivid dreams and nightmares.

They occur in nearly everyone who first uses efavirenz, but usually get easier after a few days or weeks. About 10-20% of people stop efavirenz because of the general effect on their quality of life.

Only 3% of people stop efavirenz because of more severe psychiatric symptoms. They usually can occur very early after starting treatment.

Before starting efavirenz, your doctor should give you specific information about these side effects. Efavirenz is not

Five main classes of HIV drugs:

RTIs or nukes	reverse transcriptase inhibitors - also called nucleoside or nucleotide analogues
NNRTIs	non-nucleoside reverse transcriptase inhibitors or non-nukes
PIs	protease inhibitors
EIs	entry inhibitors - CCR5 inhibitors are also entry inhibitors
INIs	integrase inhibitors

recommended during pregnancy or for women trying for a baby.

Starting on nevirapine

Nevirapine is recommended as an alternative NNRTI. This is largely because of the small risk of serious side effects.

Nevirapine has some similar side effects as efavirenz (although not the sleep or mood disturbance). This includes risk of rash and liver toxicity, which can be serious and occasionally fatal. Careful monitoring is essential.

The risk with nevirapine was found to be linked to starting treatment with a higher CD4 count (over 250 for women, and over 400 cells/mm³ for men). Whether the risk is reduced by observing these upper CD4 cut-offs is the subject of ongoing research.

A serious allergic reaction called Stevens-Johnson Syndrome (SJS) has been reported in 0.3% of people starting nevirapine compared to 0.1% in people starting efavirenz.

First-line drugs recommended by class:

Combination nukes	<i>Recommended:</i> Truvada (tenofovir + FTC) Kivexa (abacavir + 3TC) <i>Alternative:</i> Combivir (AZT+3TC) Trizivir (abacavir+AZT+3TC)
Single nukes (RTIs)	<i>Recommended:</i> abacavir (Ziagen) tenofovir (Viread) 3TC (lamivudine, Epivir) FTC (emtricitabine, Emtriva) <i>Alternative:</i> AZT ddl (didanosine, Videx) d4T (stavudine, Zerit)
NNRTIs	<i>Recommended:</i> efavirenz (Sustiva, Stocrin) <i>Alternative:</i> nevirapine (Viramune)
PIs	<i>Recommended:</i> lopinavir/r (Kaletra) fosamprenavir/r (Telzir) <i>Alternative:</i> atazanavir/r (Reyataz) saquinavir/r (Invirase) darunavir/r (Prezista) * tipranavir/r (Aptivus) * nelfinavir (Viracept)
EIs	<i>Recommended:</i> none currently in first line <i>Available:</i> T-20 (Fuzeon) * maraviroc (Celsentri) *
INIs	<i>Recommended:</i> none currently in first line <i>Available:</i> raltegravir (Isentress) *

* Currently recommended for people with drug resistance.

The most commonly used first line combinations:

Each option is used with EITHER Truvada (tenofovir + FTC) OR Kivexa (abacavir+3TC).

Drug name and comments	Side effects	Other notes
Efavirenz (Sustiva/Stocrin)		
Efavirenz is widely recommended as part of a first-line therapy. It is one pill, once-daily. Side effects, which can be significant, usually reduce after the first few weeks.	Main side effects are sleep disturbance (including nightmares), mood disturbance (including anxiety and depression) rash, liver toxicity and lipid changes. About 20% people switch to another drug over the first year.	Efavirenz should not be used during pregnancy or by women trying to conceive a baby.
Nevirapine (Viramune)		
Nevirapine is an alternative to efavirenz, but has a small higher risk of serious side effects compared to efavirenz. Nevirapine is started at one tablet a day for the first two weeks, and then one tablet twice-daily.	Main side effects are rash and liver toxicity. These only occur in the first 6-8 weeks. Any low level rash should be taken seriously. Serious rash can be fatal. If you still have a rash after the first two weeks do not increase the dose but see your doctor.	Women with a CD4 count over 250 and men with a count over 400 should not start with nevirapine.
Lopinavir/r (Kaletra)		
Kaletra is recommended as the preferred protease inhibitor. It is a twice-daily drug that includes ritonavir inside the same pill.	Main side effects are changes in lipids (blood fat), lipodystrophy (fat accumulation) which should be routinely monitored, and diarrhoea.	There is a low risk of resistance.
Atazanavir/r (Reyataz)		
Atazanavir/r is not currently approved in Europe as first-line treatment, but it is still widely used, because it is dosed once-daily and generally easy to tolerate.	Main side effects are yellowing eyes or skin in 10% of patients, relating to increased levels of bilirubin. This is only a clinical problem when total bilirubin levels increase to 60-70 mmol/L. Lipids can increase due to the boosting dose of ritonavir.	Taken with a separate dose of ritonavir (/r), unless you have high drug levels.
Fosamprenavir/r (Telzir)		
In studies fosamprenavir/r had similar results to Kaletra, but is less commonly used.	Side effects, including diarrhoea and lipids are similar to Kaletra.	Taken with a separate dose of ritonavir (/r).
Saquinavir/r (Invirase)		
Saquinavir/r has shown similar results to Kaletra. There is less comparative data to Kaletra than for fosamprenavir/r.	Side effects, including diarrhoea and lipids are similar to Kaletra. May have a lesser effect on triglyceride levels.	Taken with a separate dose of ritonavir (/r).

Regular blood tests will check for some side effects. If you have any difficulties make sure your doctor takes these seriously... including nausea and fatigue which can sometimes be serious...

Nevirapine is not routinely recommended in people with hepatitis C and HIV, because it may increase liver disease.

The reactions with nevirapine usually only occur in the first two months. Over this time, you should be monitored more carefully. Otherwise, nevirapine is reported as an easy drug to tolerate.

Starting on a boosted PI

Although UK guidelines recommend starting with an NNRTI-based combination, PI-based combinations can be just as good at getting your viral load to undetectable.

PI regimens can be less vulnerable to resistance. Some people start on a PI regimen and then switch to an NNRTI regimen that requires fewer pills later.

UK guidelines only recommend using **ritonavir-boosted** PIs. Apart from Kaletra, which has ritonavir included in the formulation, other boosted PIs need ritonavir to be dosed as a separate pill.

Using a small dose of ritonavir in these combinations provides better and more sustained drug levels.

This reduces the risk of resistance. It also reduces the number of pills and dietary requirements compared to unboosted PIs.

Some people find even small doses of ritonavir increase nausea.

People who can not tolerate ritonavir side effects, can sometimes use an un-boosted PI (usually nelfinavir or atazanavir), but they need to confirm drug levels using therapeutic drug monitoring (TDM).

Lopinavir/r (Kaletra) is the most widely used PI.

Fosamprenavir/r is an alternative to Kaletra that is used less frequently.

Atazanavir/r is a once-daily PI. It is not approved in Europe for first-time therapy, but is still used widely for this. Atazanavir/r is recommended if you want to switch drugs because of side effects. The daily dose is 300mg, boosted by 100mg of ritonavir.

If this dose causes side-effects, the ritonavir can sometimes be stopped and a slightly higher atazanavir dose (400mg) used instead.

A recent study suggested you get better drug levels with unboosted atazanavir by taking 200mg twice-daily.

Unboosted atazanavir should not be used in a combination that includes tenofovir.

Darunavir/r is a PI used for second-line PI therapy. However, a recent study showed that darunavir achieved better results compared to Kaletra in people using treatment for the first time. Guidelines may therefore recommend darunavir for first-line treatment in the future.

Saquinavir/r is an alternative to Kaletra that is used less frequently.

Tipranavir/r is a PI that is only used by people with PI-resistance.

Nelfinavir is not recommended in UK guidelines for first-line therapy, but it is sometimes chosen as the third drug if someone cannot tolerate ritonavir or for use during pregnancy.

Which nukes: Truvada vs Kivexa?

Both Truvada and Kivexa combine two nukes in one pill, that can be taken once-daily. They each have benefits and disadvantages.

Truvada = tenofovir + FTC

Kivexa = abacavir + 3TC

Neither tenofovir nor abacavir are linked to lipoatrophy, neuropathy or anaemia.

Both drugs are equally recommended in first-line treatment.

3TC and FTC are very similar drugs. They are interchangeable if individual nukes are prescribed separately rather than as a combined pill.

Tenofovir is cleared from your body by the kidneys, and monitoring for kidney toxicity, and not using tenofovir with other drugs that are cleared the same way, are important safety cautions.

Tenofovir can cause a small reduction in bone mineral density during the first 6 months, but does not seem to increase any risk of bone disease with longer use.

Abacavir can cause a side-effect called a hypersensitivity reaction that occurs in up to 7% of people.

A genetic test, called HLA B*5701, now used widely in the UK, reduces this risk. A negative result with this test does not guarantee that you will not get this reaction, but makes it much less likely.

Symptoms of the reaction include fever, rash, headache, sore throat, diarrhoea, abdominal pain, tiredness, nausea, vomiting, flu-like aches etc that get progressively worse each day.

Anyone who gets these symptoms must seek urgent medical advice with a view to stopping the abacavir.

Once stopped, abacavir must not be used by that person again, as a worse reaction can return that is potentially fatal.

AZT and Combivir

AZT is a twice-daily nuke that has been widely prescribed and studied, but is now only mainly used in first-line treatment during pregnancy.

Combivir is a fixed-dose combination of AZT and 3TC that is taken twice-daily.

The disadvantages of AZT are the side effects of anaemia, fatigue and lipoatrophy (fat loss). Lipoatrophy does not usually occur during the first six months of AZT treatment.

European guidelines do not recommend AZT as first-line choice, except for women who are pregnant or trying for a baby.

ddl

ddl is rarely used as a first-line choice, because it needs to be taken on an empty stomach (ie two hours after food). This makes dosing inconvenient. ddl is mainly used in people with drug resistance.

Triple nuke combinations

Triple 'nuke' combinations are not recommended as first-line treatment as they are less effective.

The main reason to use a triple-nuke combination is to reduce side effects related to PIs or NNRTIs or if there are interactions between these drugs and other medications (ie for TB).

Nukes that dont mix

Although one nuke can often be switched for another, there are some combinations that should not be used.

AZT and d4T	At any time
3TC and FTC	At any time
ddl and tenofovir	especially with an NNRTI
abacavir and tenofovir	in a 3-drug combo until an interaction is explained
d4T and ddl	Never during pregnancy
Triple-nuke combinations	Only two combinations: AZT+3TC+abacavir or AZT+3TC+tenofovir, can be used. Others have a high risk of failure.

Non-standard approaches

Using two nukes plus either an NNRTI or a boosted PI has produced the most effective, durable and tolerable results for combination therapy. So far, we only have limited data on other approaches.

For example, some studies have not used nukes at all. These include either two boosted-PIs, a single boosted-PI, or a PI+NNRTI combination.

Although guidelines recommend a few standard combinations, treatment is individual. If one of the recommended combinations doesn't work for you, then it is important to know there are other treatment to switch to.

New options in 2008

In 2008, treatment guidelines may change following research into new drugs.

- **Atripla** (a single pill that includes efavirenz+ tenofovir+FTC) is likely to be available in Europe in 2008. It was approved in the US in July 2006.

People taking efavirenz and Truvada, with an undetectable viral load for three months, will be able to switch to Atripla to take one less pill a day.

- **Atazanavir/r** for first-line therapy is currently being researched, and the results are expected shortly. Although atavanavir/r is widely used as first line treatment, it is not approved in Europe for this purpose.
- **Darunavir/r** was approved as a treatment for people with resistance. However, in a recent study, darunavir did better than Kaletra as first therapy, and future guidelines should reflect this.
- **Raltegravir** (an integrase inhibitor) has shown similar potency to efavirenz, but has fewer side effects or interactions with other drugs.
 Again, this drug was first studied as a treatment for people with drug resistance, but recent studies have shown it could be as good as efavirenz in people using treatment for the first time.
- **Maraviroc** (an entry inhibitor) did not do as well as efavirenz in first line therapy. Further research may show that this is a option for some patients.

How widely these new drugs will be used is also likely to be related in part to cost.

If they are more expensive than existing treatment, they may only be used when people cannot tolerate current drugs - especially if they do not show clear advantages.

Even if they are not used to start with, it is important to know that they will be options in case you need to switch treatment.

Adherence diary

Use the table below to mark when you take each drug in the first few weeks of your combination. This will help you know if you have just taken a dose - or if you are late or miss a dose. Getting everything right from the start is important.

Week date: _____

	Drugs + times (morning)	Drugs + times (evening)
Monday		
Tuesday		
Wednesday		
Thursday		
Friday		
Saturday		
Sunday		

Your personal treatment history

The next few pages include space to record important information about your own treatment and treatment history.

These have been taken from the i-Base Treatment Passport which is available free from i-Base.

If you'd like a copy of the more detailed booklet please call 020 7407 8488 or go online:

www.i-Base.info

Why keep a treatment history?

Keeping a short record of your treatment history can help in many ways:

- it can help you understand your health and treatment
- it can help if your doctor changes at your clinic
- it can help if you speak to other healthcare workers or to a treatment phoneline for advice

- it can help if you ever change hospitals or clinics, or if you want a second opinion, when on holiday or abroad, or if you move to another country.

Any treatment choice for your future care is closely linked to your previous treatment history.

This includes results from blood tests like the CD4 count, viral load and resistance tests, as well as the history of drugs you have used and your reasons for changing them. As treatment improves you could need this record for 20 years or more - and whether new treatments work may depend on previous treatment.

This record is important. If you change clinic, you should ask for your medical records to be forwarded, but this does not always happen - make sure that you have a record of your GUM or clinic number.

These pages will help provide a useful record in all these situations.

Your doctor can provide you with details to help fill in these pages but it does not replace your medical notes. All patients have the right to see their medical records and to make photocopies from them.

Immunisation record

Keeping history of vaccination and immunisation (hepatitis A and B, pneumovax, flu, tetanus and holiday vaccinations, etc) can also help.

Note that HIV-positive people usually require 'non-live' vaccinations and that you may have to ask for these specially.

Vaccination	Date	Vaccination	Date

Trials and studies

Study name and treatment received	Dates

Resistance tests

Date	Results (continue summary on notes pages if necessary)

Glossary

adherence: the term to describe taking medication exactly as it is prescribed – taking it at the right time and following any diet advice.

antibody: a protein that is part of the immune system and which recognises an infection.

antigen: infectious material produced by a virus or bacteria.

antiretroviral (ARV): an HIV drug (HIV is a retrovirus).

CD4 cells: a type of white blood cell that help your body fight infection.

first-line therapy: the first combination or HIV drugs that you use.

HAART: a term for combination therapy (Highly Active Anti-Retroviral Therapy).

mutation: a change in the structure of the virus that can stop a drug from working.

opportunistic infection (OI): an infections that occurs after your immune system has been damaged by HIV.

seroconversion: the time after HIV infection (usually a few weeks) when your body generates an immune response to HIV.

side effects: secondary effect of a drug other than the reason it is prescribed. Side effects are usually related to negative effects.

therapeutic drug monitoring (TDM): a test to measure the levels of drug in your blood

thymus: part of your immune system where new T-cells are made.

toxicity: the term for the degree to which a substance harms a person

treatment experienced: someone who has previously used anti-HIV treatments.

treatment naive: someone who has never taken any anti-HIV treatments before (people who are treatment naive can still be resistant

to anti-HIV drugs if they were infected with a drug resistant strain of HIV).

triglycerides: a type of body fat.

viral load test: A test to measure the amount of HIV in blood, but which can also check levels in other compartments like genital fluid, semen or spinal fluid. Tests can only measure down to certain levels (ie 50 copies/mL).

viral rebound: when your viral load starts to rise above detectable levels.

wild-type virus: HIV that has not developed any mutations. This is usually, but not always, the virus that you are first infected with.

Further information

If you have questions after reading this guide or would like to talk to someone about treatment contact the i-Base information service.

Positive Nation, a UK magazine is a good source of general information and support:
www.positivenation.co.uk

For further information on individual HIV drugs try the following community sites.

Non-technical basic factsheets

www.aidsinfonyet.org

A general overview on each drug

www.aidsmeds.com

An online 'drug guide'

www.tpan.com

Detailed research and references

www.aidsmap.com

Full prescribing information in most European languages and other scientific documents are available from the EMEA - use link for 'product information/human medicine':

www.emea.europa.eu













i-Base fold-out ARV guide

Antiretroviral drugs




www.i-Base.info

Drug names Recommended adult dose * Total daily pills

Nukes: nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)

Dual nukes			
Kivexa (abacavir 300mg + 3TC150mg)		One tablet, once-daily	1
Truvada (tenofovir 300mg + FTC 200g)		One tablet, once-daily	1
Combivir (AZT 300mg +3TC 150mg)		One tablet, twice-daily	2
Single nukes			
3TC (Epiriv, lamivudine)		1 x 300mg or 2 x 150mg tablets, once-daily. (150mg shown)	1 if 300mg 2 if 150mg
abacavir (Ziagen)		2 x 300mg tablets, once-daily.	2
FTC (Emtriva, emtricitabine)		1 x 200mg capsule, once-daily.	1
tenofovir (Viread)		1 x 300mg tablet, once-daily.	1
AZT (Retrovir, zidovudine)		1 x 250mg capsule, twice-daily.	2
ddl (Videx, didanosine)		1 cap, once-daily (200, 250 or 400mg). Take on empty stomach.	1
Triple nuke			
Trizivir (AZT + 3TC + abacavir)		One tablet, twice-daily	2


NNRTIs: non-nucleoside reverse transcriptase inhibitors (non-nukes)










efavirenz (Sustiva)		1 x 600mg tablet, once-daily; at night, not with a high fat meal	1
nevirapine (Viramune)		1 x 200mg tablet, twice-daily. (2 tabs once-daily possible later).	2
etravirine ** (TMC-125)		2 x 100mg tablets, twice daily, Take with food.	4

*All doses need to be confirmed by your doctor and pharmacist as other doses are possible and not all are licensed in Europe.



** Indicates a drug not licensed in Europe at time of printing. Images approximate to actual size. T

Fixed dose NNRTI + dual nuke combination


Atripla ** (efavirenz + Truvada [FTC + tenofovir])		One tablet, once-daily - switch option after viral suppression. Guidance as for separate drugs.	1
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lopinavir/r (Kaletra)		2 x 200mg tablets, twice-daily. Take with food.	4
fosamprenavir/r (Telzir)		1 x 700mg tablets + 100mg RTV, twice-daily. Take with food.	2 + 2 caps ritonavir
saquinavir/r (Invirase)		2 x 500mg caps + 100mg RTV, twice-daily. Take with food.	4 + 2 caps ritonavir
atazanavir/r (Reyataz)		2 x 150mg caps + 100mg RTV, once-daily. Take with food.	2 + 1 cap ritonavir
darunavir/r (Prezista)		2 x 300mg caps + 100mg RTV, twice-daily. Take with food.	4 + 2 caps ritonavir
tipranavir/r (Aptivus)		2 x 250mg caps + 200mg RTV, twice-daily. Take with food.	4 + 4 caps ritonavir
nelfinavir (Viracept)		5 x 250mg tabs, twice-daily. Take with food.	10
indinavir/r (Crixivan)		2 x 400mg caps + 100mg RTV, twice-daily.	4 + 2 caps ritonavir
ritonavir (RTV) (Norvir)		100mg capsules used at different doses to boost other PIs.	Depends on PI

EIs: entry inhibitors, including CCR5 inhibitors

T-20 (Fuzeon, enfuvirtide)	 not actual size	90mg injection under the skin, twice-daily	2 injections daily
maraviroc (Celsentri, Selzentry)		1 x 300mg, twice-daily (150mg or 600mg dose needed with some ARVs due to interactions).	2

INIs: integrase inhibitors

raltegravir ** (Isentress)		1 x 400mg tablet, twice-daily.	2
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How to access our services

Call Free on **0808 800 6013**

Treatment Information Phoneline

Open Mon–Wed: 12.00–16.00



Visit our website at www.i-Base.info

- **adherence – could you use some support?**
- **side effects – or about anything in this booklet**
- **trials – discuss the benefits and risks of joining a trial or study**
- **information service – we can send you the latest research**

Publications

All i-Base publications are available free.

Treatment guides are written in everyday language.

HTB is written in more technical medical language.

Please send me: (please write clearly)

- Introduction to Combination Therapy (this guide)
- Changing Treatment: ...if treatment fails: (second-line therapy and drug resistance)
- HIV, Pregnancy and Women's Health
- Guide to HIV and Hepatitis Coinfection
- Guide to Avoiding and Managing Side Effects
- Treatment Passport – small booklet to record your treatment history
- HIV Treatment Bulletin (HTB)

Publications in other languages are available in pdf format at www.i-Base.info

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