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# hiv therapy

fourth edition 2008



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**Written by Michael Carter**

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# hiv therapy

**The British HIV Association (BHIVA) is the UK's professional body for doctors who care for people with HIV. BHIVA produces guidelines on how the medical care of people with HIV should be managed. Recently, BHIVA agreed revised practice guidelines for 2008 on the use of drugs to treat HIV infection.**

**This booklet has been written to help you decide what questions to ask your doctor about any course of treatment you might be considering. It is not intended to replace discussion with your doctor about treatment.**

# contents

## BHIVA HIV treatment guidelines

1

## What is HIV therapy?

3

## When should anti-HIV therapy be started?

4

- If you have contracted HIV very recently 4
- If you have established (chronic) infection but do not have any symptoms 6
- People with symptoms of HIV disease or AIDS 7

## What to start therapy with

9

- Preferred combination: efavirenz (*Sustiva*) plus *Truvada* or *Kivexa* 9
- Preferred NRTIs 10
- Alternative combination: choice of NNRTI 11
- Alternative combination: a boosted protease inhibitor 12

## When to change therapy

14

- Changing drugs after more than one treatment failure

15

## Taking your treatment

18

## Summary

20

## Glossary

21

# 1 BHIVA HIV treatment guidelines

This booklet is a summary of the BHIVA HIV treatment guidelines: a set of recommendations about how HIV therapy should be used to treat people with HIV infection in the United Kingdom. Several of the subjects covered within the guidelines are not included in this booklet, a couple of examples being the side-effects of treatment including lipodystrophy, the blood and body fat changes which can affect people taking HIV therapy; and detailed information on the treatment of HIV if you also have hepatitis B or hepatitis C virus (or both) (for more information on these subjects see the booklets in this series *Lipodystrophy*, and *HIV and hepatitis*).

If you would like to read the 2008 BHIVA treatment guidelines in full, they are available on [www.bhiva.org](http://www.bhiva.org).

BHIVA comes up with its own recommendations through a consensus-building exercise where advice is based mainly on evidence from clinical trials, and where there is no such evidence, on the opinion of HIV experts. This is because there is not enough scientific research to answer all the questions about the best use of HIV treatments. Research in the HIV field moves unusually quickly, which means that the guidelines summarised in this booklet should be seen as “best practice” based on what we know

about HIV infection and its treatment at the moment.

These guidelines are not a recipe book for treating your HIV infection. HIV always requires individualised care, which is based both on your past and present state of health, and on the wider factors which influence your daily life.

### 3 What is HIV therapy?

Drugs given to treat HIV are also called antiretrovirals. To ensure that antiretrovirals have a powerful and long-lasting effect against HIV, it is necessary to take a combination of three (sometimes more) anti-HIV drugs.

Currently available HIV therapy does not eliminate the virus from the body. Instead, it can prolong life and good health by suppressing HIV replication and therefore reducing the harmful effects of HIV on the immune system.



## When should HIV therapy be started?

There is no clear evidence on when is the best time for you to start taking anti-HIV drugs. This means that you must weight up with your doctor, the likely benefits and risks for you of taking treatment now, as opposed to waiting until later. The current view is that treatment is clearly beneficial:

- If you have symptoms of HIV or AIDS.
- If you have a CD4 cell count around 350.

### **If you have contracted HIV very recently**

The six month period which follows immediately after you contract HIV is called primary infection. There is no proof

that starting treatment at this time will definitely lead you to live a longer, healthier life.

Some doctors believe, however, that this time may offer a unique chance to intervene which may be lost later in infection as your immune system sustains ongoing damage, and so may be less able to respond to HIV itself.

This potential benefit has to be weighed against the risk of you getting side-effects of the drugs, finding that treatment reduces your quality of life, and the possibility that if the treatment you take stops working effectively against HIV, you

may be left with drug resistant virus.

The results of small studies looking at the risks and benefits of treatment soon after infection with HIV are far from conclusive. Some people who took anti-HIV treatment very soon after infection seem to have maintained extremely low levels of HIV, even after stopping treatment. But on the other hand, others who have tried the same strategy have not had this response. Because there is a lack of clarity, a much larger clinical trial is currently looking at the benefits of treatment at this stage. Its results will be available in a few years.

Until these results are available, the only people who are recommended to consider treatment soon after they've been infected with HIV are those with:

- Any AIDS-defining illness.
- Neurological (brain) conditions that are related to HIV.
- A CD4 cell count that is below 200 for three months or more.

However most people do not find out that they have been infected until they develop symptoms many months or years later.

## If you have established (chronic) HIV infection but do not have any symptoms

You should certainly start anti-HIV treatment before your CD4 count falls below 200. If you start treatment when your CD4 count is below 200, you face a greater risk of ill health and even death in the short-term, than if you start while your CD4 count is still above 200.

There is now a consensus that there are benefits to starting anti-HIV treatment when your CD4 cell count is around 350. Your doctor should discuss starting anti-HIV treatment when your CD4 cell count is around this figure and you are

recommended to start treatment as soon as you are ready. There is good evidence that starting treatment when your CD4 cell count is in the region of 350 reduces your risk of developing not only HIV-related illnesses but also other serious illnesses as well, including heart, kidney and liver disease and some cancers.

Treatment with a CD4 cell count of 350 is particularly encouraged for people who have any of the following characteristics:

- A viral load above 100,000.
- A rapidly falling CD4 cell count (80 cells or more a year).
- Any HIV-related illnesses.

- Coinfection with hepatitis B virus or hepatitis C virus (or both).
- Age over 50 years.
- A risk of heart disease.
- A partner who is HIV-negative.

Some doctors also believe that starting treatment at this time is advisable for people of African origin who have kidney disease.

If you are advised to start treatment but choose not to, then you should review your decision regularly and have your CD4 count and viral load monitored more frequently than usually recommended.

## People with symptoms of HIV disease or AIDS

Everybody who has been diagnosed with an AIDS-defining infection or cancer is recommended to start anti-HIV treatment. An exception is tuberculosis (TB) if your CD4 cell count is above 350 (see the booklet in this series, *HIV and TB* for more details).

In most cases, anti-HIV treatment will be started once you've finished treatment for your infection. This is because anti-HIV drugs can sometimes interact with medicines used to treat infections. There can also be a risk of a set of unpleasant symptoms called an immune reconstitution

inflammatory syndrome if you take treatment for some infections and anti-HIV therapy close together.

If you have been diagnosed with lymphoma, you should start anti-HIV treatment as soon as you commence chemotherapy.

## 9 What to start therapy with

### **Preferred combination: efavirenz (*Sustiva*) plus either tenofovir and FTC (*Truvada*) OR abacavir and 3TC (*Kivexa*)**

If you are starting anti-HIV treatment for the first time, you are recommended to take the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz (*Sustiva*) with either the nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) combination pill *Truvada* (this contains FTC and tenofovir) or the NRTI combination pill *Kivexa* (this contains abacavir and 3TC).

There is good evidence that efavirenz has a powerful and long-lasting anti-HIV

effect. It also causes relatively few side-effects and is easy to take.

But a major disadvantage of efavirenz is that it is easy for HIV to develop resistance to it. It can also cause neurological side-effects. These normally only last a few weeks, but some people find that symptoms such as headache, bad dreams, feeling disoriented and depression are longer-lasting and problematic.

You should not start treatment with efavirenz if you are thinking of becoming pregnant as there is a theoretical risk that it can cause birth-defects. If you are already taking efavirenz and become

pregnant, you should contact your HIV clinic as soon as possible for advice.

## Preferred NRTIs

There are two NRTI combination pills preferred for use in people starting treatment.

FTC (emtricitabine, *Emtriva*) and tenofovir (*Viread*) are combined in the pill *Truvada*. These drugs have a powerful and long-lasting anti-HIV effect and are easy to take.

There is some evidence linking tenofovir with an increased risk of kidney disease, particularly in people who have pre-existing kidney problems.

The alternative is *Kivexa*, a combined pill containing abacavir and 3TC.

About 5% - 8% of people who start treatment with abacavir experience a severe allergic or hypersensitivity reaction. This has been linked to a particular gene called HLA-B\*5701 and you should have a test to see if you have this gene before starting treatment with abacavir. If your test is positive you should not take abacavir. If your test is negative it is unlikely that you will have a reaction to abacavir, but if you develop symptoms including rash, tummy problems, sickness, and a feeling of being generally unwell soon after starting abacavir, you should contact your HIV clinic as soon as possible.

*Kivexa* has a powerful and long-lasting anti-HIV effect and is easy to take. But there is some evidence that people who have a high viral load are less likely to experience a fall in their viral load to undetectable levels if they take abacavir rather than tenofovir, so if you have a high viral load you shouldn't take it.

Abacavir was linked in one big study with an increased risk of heart attack, particularly in people with existing risk factors for heart disease. But the results of this study are limited, not least because it did not examine the heart attack risk of either tenofovir or FTC.

*Kivexa* is recommended as an alternative

to *Truvada*, particularly for people with kidney disease or a risk of kidney disease.

*Combivir* (AZT and 3TC) is not recommended for people starting anti-HIV treatment. This is because AZT has been associated with fat loss (lipoatrophy). But it might be a good choice if you are pregnant or thinking of becoming pregnant. This is because there is evidence AZT is good at preventing mother-to-child transmission of HIV.

### **Alternative combination: choice of NNRTI**

The NNRTI nevirapine (*Viramune*) is an alternative to efavirenz, but it is only



recommended for certain groups of people. These include women who wish to become pregnant, as there is good evidence that nevirapine is good at preventing mother-to-child transmission of HIV. Nevirapine might also be an option if you cannot tolerate the neurological side-effects of efavirenz.

Nevirapine can cause a rash and potentially dangerous liver side-effects. To reduce the risk of these, women should not start anti-HIV treatment with nevirapine if their CD4 cell count is above 250, and men should not start treatment with this drug if their CD4 cell count is above 400.

## **Alternative combination: a boosted protease inhibitor**

A boosted protease inhibitor (these protease inhibitors have their anti-HIV effect enhanced by taking them with a small dose of ritonavir) is an alternative to efavirenz.

Boosted protease inhibitors are recommended as an alternative to efavirenz if you:

- Are infected with HIV that is resistant to NNRTIs or NRTIs.
- Are pregnant or are thinking of becoming pregnant.

- Are unable to tolerate the neurological side-effects of efavirenz or have a history of depression.
- Are likely to find it difficult to take your HIV medicines properly. In these circumstances, there is less risk of resistance with a boosted protease inhibitor than with efavirenz.

The recommended boosted protease inhibitors are:

- lopinavir/ritonavir (*Kaletra*). This is the only boosted protease inhibitor which includes ritonavir in the same pill.
- fosamprenavir (*Telzir*) plus ritonavir.
- saquinavir (*Invirase*) plus ritonavir.
- atazanavir (*Reyataz*) plus ritonavir.
- darunavir (*Prezista*) plus ritonavir.

## When to change therapy

The goal of anti-HIV treatment is an undetectable viral load (below 50 copies/ml of blood in the tests used in most HIV clinics).

If your viral load is above this level then HIV is continuing to reproduce.

Your treatment is also considered to be failing if you have achieved an undetectable viral load and then have two viral load tests at least two weeks apart which both show that viral load is above 50.

If there are other drugs available to you that give you the chance of getting an undetectable viral load, and you will be able to tolerate these drugs and take them

properly, then you should consider switching therapy.

Your choice of replacement drugs should also be guided by the results of a resistance test and your previous treatment history.

Sometimes your viral load may rise to just above the detectable level and then fall back below on the next test. This is called a "blip" and means that your viral load should be re-tested as soon as possible, ideally within two weeks. Though one-off blips may be caused by a problem with viral load testing itself, they should also be a trigger to consider other possible causes,

such as drug interactions, adherence problems, illnesses or vaccinations. Regular blips may be a sign that your treatment is more likely to fail.

If your treatment is being changed because of side-effects, but your viral load is below 50, it is okay to switch only the drug(s) causing problems.

If you have had problems taking your drugs regularly, known as adherence, your failing treatment regimen should ideally be replaced with drugs that are easier to take, and support with adherence should be provided to you. For more information on the steps you can take to improve your

adherence see the booklet in this series called *Adherence*.

## **Changing drugs after more than one treatment failure**

Doctors often make a distinction when talking about people who need to change their anti-HIV drugs for the first time and those who've already made changes before because of the failure of their treatment to control viral load. The term "salvage therapy" is sometimes used to describe treatment if you have already taken drugs from all the major anti-HIV drug classes.

Ideally your new treatment should include two, preferably three new drugs, with at

least one from a new class.

A number of new anti-HIV drugs have recently become available. It is harder for HIV to become resistant to some of these drugs than many of the older anti-HIV drugs. Some of the new drugs work against HIV in a completely different way to older anti-HIV drugs. These drugs are therefore important new treatment options for people who have taken a lot of anti-HIV drugs in the past and have drug resistant virus.

The new anti-HIV drugs that are important treatment options for people who've taken a lot of anti-HIV drugs in the past are:

- darunavir (*Prezista*)/ritonavir.
- maraviroc (*Celsentri*).
- raltegravir (*Isentress*).
- etravirine (*Intelence*, approval expected later in 2008).

T-20 (enfuvirtide, *Fuzeon*) has been available for a number of years, and it is an important treatment option for some people.

Doctors now believe that better standards of HIV care, for example the use of resistance tests and these new drugs mean that an undetectable viral load should be the goal of everybody taking anti-HIV treatment.

But even if you cannot get an undetectable viral load, even quite small falls in viral load can mean that you have a reduced risk of illness or death. Maintaining your CD4 cell count is also likely to be a priority in these circumstances.

Treatment breaks (often called structured treatment interruptions or drug holidays) are not recommended, particularly if you are taking “salvage therapy.”

“Recycling” drugs (taking a treatment that you’ve previously developed resistance to) might be of benefit in some circumstances, and there is evidence that 3TC has some anti-HIV effects and benefits even if the virus has developed resistance to it.

In some instances it is necessary to remain on a “failing” combination in the short-term until an effective combination can be found. You’ll need expert management, which takes into account your individual treatment history and drug resistance profile.

The success of your anti-HIV drugs requires a very high level of dedication from you. Adherence is the term used to describe taking your anti-HIV drugs exactly as prescribed, with no missed or late doses, and eating the correct type of food at the right time in relation to your drugs if that's required. You should aim to take every dose of your medicine. Missing even a few doses can cause your drugs to fail and there's good evidence that adherence levels of over 90-95% are what's needed for you to get the best response. This means missing no more than one dose a month if you are taking once a day therapy, or two doses a month if you are taking your anti-HIV drugs twice a day.

Adherence support should be part of the routine care you receive from your clinic. The following issues are important elements within effective adherence and should be considered periodically as part of your HIV care, and whenever you start a new HIV drug combination:

- Your motivation to start and continue with your treatment.
- Your understanding of adherence and drug resistance.
- The impact of treatment on your lifestyle and well-being.
- Your mental health.
- Risk of side-effects, and their management.

- The risk and benefits of treatment.
- That you have the information you need to be able to take your treatments, including information in written form.

Pill boxes have been shown to help improve adherence. HIV clinics are often able to provide free pill boxes with separate compartments for each dose you have to take so you can keep track of the doses you've taken.

For more information, see the booklet *Adherence* in this series.



- People with HIV always require individualised care.
- Currently available HIV therapy does not eliminate HIV from your body.
- If your CD4 cell count is around 350, or if you are ill because of HIV, you are advised to take treatment.
- You are recommended to start treatment with efavirenz (*Sustiva*) with either *Truvada* (tenofovir and FTC) or *Kivexa* (3TC and abacavir).
- HIV therapy which is not suppressing viral load to undetectable levels should be changed if there are other drugs available which seem likely to achieve this.
- If you've taken a lot of anti-HIV drugs before then you might benefit from some new types of anti-HIV drug.
- To work, anti-HIV drugs have to be taken properly. This is more likely to happen if you have taken part in decisions about your treatment and are supported in, and committed to, taking it.

## 21 Glossary

### **adherence**

The act of taking treatment exactly as prescribed.

### **antiretroviral**

A substance that acts against retroviruses such as HIV.

### **boosted protease inhibitor**

A protease inhibitor that has its anti-HIV effect increased by taking it with a small dose of ritonavir (another protease inhibitor).

### **CD4**

A molecule on the surface of some cells onto which HIV can bind. The CD4 cell count reflects that state of the immune system.

### **hypersensitivity**

An allergic reaction.

### **lipoatrophy**

Fat loss.

### **lipodystrophy**

A disruption in the way the body produces, uses and distributes fat.

### **NNRTI**

Non-nucleoside reverse transcriptase inhibitor. The family of antiretrovirals which includes efavirenz, etravirine and nevirapine.

### **NRTI**

Nucleoside reverse transcriptase

inhibitor. Family of antiretrovirals to which 3TC, abacavir, AZT, ddI, d4T and FTC belong.

### **NtRTI**

Nucleotide reverse transcriptase inhibitor. Family of antiretrovirals which includes tenofovir.

### **protease inhibitor**

Family of antiretrovirals that includes atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir and tipranavir.

### **regimen**

A drug or treatment combination and the way it is taken.

### **resistance**

A drug resistant HIV strain is one which is less susceptible to the effects of one or more anti-HIV drugs because of the way it has evolved.

### **resistance test**

Blood test which detects resistance to anti-HIV drugs.

### **salvage therapy**

Any treatment regimen used after a number of earlier treatment combinations have failed.

### **undetectable viral load**

A level of viral load which is too low to be picked up by the viral load test being

used. Most clinics use tests with a lower-limit of 50°, although some use a test with a limit of 40°.

**viral load**

The amount of virus in the blood.

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**THIS QUESTIONNAIRE IS ANONYMOUS AND CONFIDENTIAL.**

Below are a series of statements. Please tick the box you agree with.

This booklet has:

- Increased my awareness of the most recent guidelines published by the British HIV Association (BHIVA) on the use of drugs to treat HIV infection
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- Before I read this booklet I already had a good understanding of the BHIVA guidelines
- This booklet will help me talk to my doctor about my HIV treatment
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- Are there any other issues that you would like to see covered in this booklet?

- 
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**Can we ask you a few more questions? You don't have to answer these but if you do it will help us make sure that our information reaches the people who need it most.**

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**NAM**

Lincoln House  
1 Brixton Road  
London  
SW9 6DE  
UK

**tel** +44 (0) 20 7840 0050  
**fax** +44 (0) 20 7735 5351

**email** [info@nam.org.uk](mailto:info@nam.org.uk)  
**website** [www.aidsmap.com](http://www.aidsmap.com)

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