

Side-effects

2013 Second edition



Acknowledgements

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Side-effects

This booklet provides information about the possible side-effects of HIV treatment. All drugs, including those used to treat HIV, can cause unwanted side-effects. You may be reading this because you are worried about such side-effects or because you have already experienced them. The information here aims to help you understand, avoid and deal with side-effects.

Not everyone experiences side-effects, and just because a drug's side-effect is discussed in this booklet does not mean that you will develop it if you take that drug. Even if side-effects develop, they are usually mild, temporary or treatable.

It is important to talk to your HIV doctor or another member of your healthcare team about any concerns you have about side-effects, or any symptoms you are experiencing. This booklet aims to help inform that discussion.

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HIV treatment - a longer and healthier life

Good medical care, including access to anti-HIV drugs, can mean a long and healthy life for people living with HIV. Current HIV treatment does not cure HIV, but keeps it under control allowing the immune system to stay strong.

The amount of illness and death in people with HIV fell dramatically after combinations of three anti-HIV drugs started to be used in the mid-1990s. There have been further improvements in HIV treatment and care since then. Research has shown that HIV treatment means someone with HIV has a more-or-less normal life expectancy. To put it very simply - **HIV treatment works!**

To get the maximum benefit from HIV treatment you need to take your treatment in the way your doctor or pharmacist has advised every day. For most people starting HIV treatment, this means taking one or two pills once a day. Many people will forget a dose at some point, but most anti-HIV drugs will still work if you miss an occasional dose and take it a few hours later.

You're most likely to get the greatest benefit from your HIV treatment if you start taking treatment before HIV has done too much damage to your immune system. In the UK, standards for HIV treatment and care are set and monitored by the British HIV Association (BHIVA), the professional association for HIV doctors and other healthcare professionals.

HIV treatment - a longer and healthier life

BHIVA's guidelines on HIV treatment currently recommend that adults start treatment when their CD4 cell count is around 350. Starting treatment at this time has been shown to reduce the risk of HIV-related illness and of some other serious illnesses, such as heart, kidney and liver disease as well.

In some situations, it may be recommended that someone starts treatment sooner, while their CD4 cell count is still above 350. These include:

- if you have an HIV-related illness
- if you have hepatitis
- if you need treatment for cancer
- if you are over 50, or
- to reduce the risk of passing HIV on.

Once you've started treatment, it is important to take all the doses of your anti-HIV drugs correctly. This will mean that there is very little chance that your drugs will stop working because your HIV has become resistant to them. You can find out more about taking HIV treatment in the booklet in this series, *Adherence & resistance*.

Like any other medicines, the drugs used to treat HIV can have unwanted secondary effects that are sometimes unpleasant or can even make you unwell. These are called side-effects. Sometimes they are also called secondary effects, adverse events or adverse reactions.

It's important to stress that the benefits of HIV treatment by far outweigh the risk of side-effects.

The anti-HIV drugs used today cause far fewer side-effects than those that were commonly used in the past. The choice of drugs is much greater now and something can usually be done if your anti-HIV drugs do cause side-effects. You don't have to 'grin and bear' side-effects.

This booklet provides you with information about HIV treatment side-effects, the likelihood they will happen, how to minimise the risk of them developing, how to manage them if they do occur and what to do if you develop a serious side-effect.

Safeguards against side-effects

HIV mainly infects cells in the immune system called CD4 cells. When someone has HIV, the number of CD4 cells drops gradually but continually and the immune system is weakened. HIV treatment works by interrupting this process. To stop HIV reproducing, it is necessary to take a combination of anti-HIV drugs that each target the virus in a slightly different way. These drugs are very effective in working against HIV, but they can also have unwanted side-effects.

It isn't just anti-HIV drugs that cause side-effects – all medicines (including drugs bought without a prescription 'over the counter' and complementary and alternative medicines,

Safeguards against side-effects

which include so-called 'natural' and 'herbal' medicines) can have unwanted side-effects.

Side-effects can also happen because someone is taking several different drugs which interact with each other. It is important that your doctor and pharmacist know about all other medicines and drugs that you are taking - this includes those prescribed by another doctor, over-the-counter remedies, herbal and alternative treatments, and recreational drugs.

Every anti-HIV drug now in use has been through years of research. This includes clinical trials with hundreds, if not thousands, of people with HIV. These trials are run to make sure that the drugs work against HIV and are safe to use. For a drug to be approved for use

it has to be shown that the benefits of using it outweigh the side-effects that it causes.

Most of the side-effects identified in clinical trials tend to be quite mild - for example diarrhoea, feeling sick, or headache - and they are often temporary. But even mild side-effects can affect your quality of life, so it is important to know about the risk of them.

Sometimes more serious side-effects are identified in clinical trials and research. A particularly serious, even dangerous, side-effect can be an allergic reaction to a drug. However, these are rare.

You can find more detailed information on this on page 36 - it is important to know what to look out for.

Timing of side-effects

Some side-effects appear soon after treatment with a drug is started as the body adjusts to treatment with the new drug. Such side-effects often lessen, become manageable or go away completely after a few days, weeks or months. They are often called short-term side-effects.

Other side-effects may only appear after a number of months or even years of treatment with a drug, and these are called long-term side-effects.

Drugs sometimes cause side-effects that were not identified during the research into their development and only become clear when the drug is being taken by lots of people for

a longer period. It makes good sense to tell your doctor about any unusual symptoms you develop so the cause can be investigated and you can take the most appropriate action.

Side-effects are not always something you feel. Doctors will look for the signs of some side-effects when they run blood and other tests at your HIV clinic appointments. This helps them check for any side-effects you may not even notice. It is important you attend your regular clinic appointments so you are monitored for these side-effects.

Who gets side-effects?

Anti-HIV drugs can cause side-effects in anyone. But that doesn't mean that you will definitely experience side-effects – in fact many people who take HIV treatment don't have any side-effects at all.

The type and severity of side-effects can also vary between people.

Some people find that, although they have side-effects, these are mild and they can live with them without distress or inconvenience.

Other people find that they initially experience side-effects that then become less severe or go away completely.

However, a small number of people find that side-effects are a permanent feature of a particular HIV drug and affect their quality of life, even going so far as causing physical or mental illness.

Your risk of developing some side-effects can be affected by a number of factors related to who you are.

For example, some people have a particular gene (HLA-B*5701) which puts them at risk of a severe allergic (hypersensitivity) reaction to the anti-HIV drug abacavir. There is a test to find out if you have that gene, which your doctor will arrange if you are considering treatment with abacavir. If you do have the gene, you must not take abacavir (see page 36 for more information).

Who gets side-effects?

Another such factor is race. For example, some people process efavirenz more slowly than others. This is thought to be linked to a genetic variation which is common in black African people. It can increase the risk of side-effects.

Sometimes, taking other medications or drugs, including over-the-counter, herbal or recreational drugs, at the same time as anti-HIV drugs can increase the chances of having side-effects.

And how you live your life might also affect your risk of some other side-effects. Some anti-HIV drugs, for example, can cause increases in blood fats, and this could be made worse if you eat lots of high-fat foods. There is some concern that treatment with some anti-HIV

drugs might increase the risk of cardiovascular disease, and this can be a real concern for people with other risk factors for heart disease such as smoking or a family history of heart disease.

Other HIV drugs have been linked with liver problems, and these can also be caused by drinking too much alcohol or using recreational drugs. Being infected with hepatitis B or hepatitis C can also mean that you have an increased risk of developing liver problems if you are taking certain anti-HIV drugs.

There are actions, many of which have other health benefits as well, that you can take to reduce the risk of developing certain side-effects. These include eating a balanced diet

Taking control of side-effects

with lots of fresh fruit and vegetables and not too much fat, taking exercise, not smoking, and not drinking too much alcohol.

If you have risk factors for side-effects (for example, a family history of heart disease or infection with hepatitis B or C), it is important that your doctor knows about them. This will enable you and your doctor to find the most suitable anti-HIV drugs for you. NAM's online tool, *Talking points* (www.aidsmap.com/talking-points), can help you prepare for this discussion with your doctor by taking you through the health and lifestyle factors that might affect your choice of anti-HIV drugs.

Taking control of side-effects

Side-effects can be annoying, inconvenient, distressing and sometimes even frightening. But it can be helpful to know that it is not inevitable that you will experience them. You can often take action to reduce the risk of side-effects in the first place. And if you do experience side-effects, there is nearly always something you can do about them.

Your approach to side-effects

Having a realistic approach to side-effects can be a good place to start. Although it is important to recognise that HIV treatment can cause side-effects, it is equally important to acknowledge that:

Taking control of side-effects

- They do not always happen. You may not have any side-effects at all.
- The anti-HIV drugs that are most widely used today don't cause the severe side-effects that earlier HIV drugs caused.
- HIV treatment can give you the chance of a normal lifespan. Putting off starting treatment because of a fear of side-effects can increase your risk of becoming ill. Starting treatment when you have a weak immune system might even increase your risk of side-effects.
- Most side-effects are mild and often lessen, go away completely, or can be controlled with other treatment.
- Some side-effects can be controlled safely with other treatment.
- HIV treatment is meant to make you better. You do not have to put up with side-effects. If you cannot cope with a side-effect, the chances are that something can be done about it.
- There are now lots of HIV treatment options available and you might be able to switch to a treatment that does not cause the side-effect you are experiencing.
- Stopping your treatment without your doctor's help can lead to other treatment complications. If you are not happy with your HIV treatment because of the side-

Taking control of side-effects

effects, you should discuss this with your doctor as soon as possible.

Finding out about side-effects

If you are about to start or change HIV treatment, finding out about the side-effects that anti-HIV drugs can cause might help you choose the most suitable combination of drugs for you. But remember, just because the side-effects are listed in information about the drug does not mean you will experience them.

Later in this booklet are details of some of the most commonly used HIV treatment combinations and details of the side-effects that these drugs can cause. There are also details of what you can do about these side-effects.

You can also find out about side-effects on NAM's website, www.aidsmap.com. You can use NAM's online tool, *My drugs chart* (www.aidsmap.com/my-drugs-chart), to find out about common and rare side-effects for all the anti-HIV drugs currently available.

Talking about side-effects

It is important to talk to your doctor, HIV specialist nurse or pharmacist about the risk of side-effects and how they might affect you. During this discussion it's a good idea to mention your medical history, that of your family and any lifestyle issues that might affect your risk of side-effects. It is also important to tell your GP of any HIV medicines that you are taking, to prevent them prescribing a drug which may cause harmful interactions

Taking control of side-effects

Things you need to tell your HIV healthcare team include:

- Known or suspected allergies to any other medicines, including creams, eye drops and inhalers.
- Other important health conditions – for example, heart, liver or kidney disease, or mental health problems such as depression.
- Use of any other drugs – including prescription, over-the-counter, complementary (herbal) or recreational drugs.

If you are worried about a particular side-effect, tell a member of your healthcare team. They should be able to give you more information about this side-effect and talk

through your concerns with you. They may be able to recommend an alternative treatment, or ways of reducing the risk or impact of the side-effect.

Your doctor or the pharmacist will tell you if the medicines you are prescribed might cause any potentially dangerous side-effects and what the symptoms of these can be. If there is anything you do not understand, it's a good idea to ask for more information. You should be given the contact details of someone to contact when the clinic is closed, in case you think you might be experiencing potentially dangerous side-effects.

Starting or changing HIV treatment is rarely done as an emergency and it is highly unlikely

Taking control of side-effects

that you will have to make an instant decision about your HIV treatment. If it's possible, you may find it helpful to start treatment at a time when you have fewer other stresses in your life and you can give yourself time to cope with any early side-effects that you might experience. You may find NAM's online tool, *Get set for HIV treatment* (www.aidsmap.com/getset), useful in helping you prepare for starting treatment.

Your lifestyle and side-effects

The way you look after your health can help reduce the risk of developing some side-effects, or make side-effects less severe if they do occur.

Starting HIV treatment is likely to be a major event in your life, so be realistic about your

ability to cope with potential side-effects. Changing treatment can happen with very few problems, but sometimes it can also be stressful. If possible, it makes good sense not to plan other major life changes that coincide with starting or changing treatment.

It is also useful to remember some general health tips.

- Make sure you eat! And think about what you eat. A healthy, balanced diet is essential to overall health. A good place to find out about eating well is the NAM booklet, *Nutrition*. Your HIV clinic will be able to refer you to a dietitian who can offer advice and information about your diet.

Taking control of side-effects

- Sleep is essential to good physical and mental health. If you are having problems sleeping, help is available from your HIV clinic or your GP.
- Feeling able to cope with life's ups and downs is just as important as being in good physical health. You can find out about looking after your mental health in the NAM booklet, *HIV, mental health & emotional wellbeing*.
- Regular exercise is important. It will make you feel better and can also reduce the risk of developing some serious illnesses. You may want to ask at your HIV clinic if they can refer you to exercise schemes for people with HIV, or ask your GP about exercise on prescription if you are unsure about starting an exercise programme.
- Smoking causes many health problems, including lung cancers, heart disease and strokes. If you smoke, try to stop. The NHS offers free help if you want to stop smoking. Talk to your doctor for more information.
- Watch how much alcohol you drink. Regularly drinking more than the recommended number of units can cause health problems such as liver disease, heart disease and stroke.
- Be careful about using recreational drugs. If you're concerned about either your alcohol or drug use, you might want to mention this

Taking control of side-effects

to someone at your HIV clinic, or your GP, as help will be available.

Changing experience of side-effects

Many people taking HIV treatment will experience some sort of side-effect at some time. But most of these side-effects are mild, temporary or treatable.

So it might be useful to remember that even if you are having a difficult experience of side-effects, or feeling low because of them, it is highly unlikely that this will always be your experience.

But it's equally important to remember that you don't have to put up with side-effects, or deal with them on your own. HIV treatment

is intended to keep you well. If a side-effect is affecting the quality of your life, it makes good sense to tell your HIV doctor, nurse or pharmacist – help will be available.

It's particularly important to do something about a side-effect if it means you are less likely to take your treatment at the right time, or in the right way (often called adherence). Good adherence is key to your HIV treatment being effective. But it can be harder to take your treatment if you're expecting it to make you feel less well.

Reporting side-effects

It's important to tell your doctor about any symptoms that you are experiencing. Your doctor will discuss with you whether these are

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actually side-effects and, if so, will be able to give you advice and help you make a decision about what to do about the symptom. You may find it helpful to keep a record of the symptoms you're having – how often you have them and how long they last, when they occur and how severe they are, for example. Try to explain to your doctor the effect these symptoms have on your day-to-day life. It's important your doctor knows if they stop you from doing the things you normally do, or if they are affecting your mental health.

You can also report side-effects to the government agency in charge of monitoring the safety of medicines using a facility called the Yellow Card Scheme.

You can do this online at www.yellowcard.gov.uk. You'll be asked to fill out a form, which is confidential.

If your side-effect has been caused by an anti-HIV drug you'll also be asked to provide some additional information such as your CD4 cell count, viral load, previous illnesses and previous side-effects. This information helps researchers to understand if the risk of side-effects is connected with any particular factors, but bear in mind that the information you give will not be reported to your healthcare team, so you should talk to your doctor about any side-effects you are concerned about.

HIV treatment combinations and their side-effects

The likelihood of having a side-effect

Side-effects are often described in the following categories:

- *very common*. This means that more than one in ten people taking the medicine are likely to have the side-effect.
- *common*. This means that between one in ten and one in 100 people are affected.
- *uncommon*. This means that between one in 100 and one in 1000 people are affected.

- *rare*. This means that between one in 1000 and one in 10,000 people are affected.
- *very rare*. This means that fewer than one in 10,000 people are affected.
- *not known*. This means that it's not been possible to estimate the number of people affected.

In this booklet, we list the very common or common side-effects for individual drugs. We have only included the uncommon, rare or very rare side-effects if they are potentially dangerous.

Starting treatment for the first time?

The drugs recommended for people starting

HIV treatment combinations and their side-effects

HIV treatment for the first time generally have few side-effects. It is particularly good to know that they do not cause the more serious side-effects that were caused by some of the older HIV drugs – these drugs are now only used rarely because other drugs are now available that are safer and often easier to take.

Because of this, it's less common than it used to be for people to have to change their HIV treatment because of side-effects. Many people will probably be able to take the currently available first-choice anti-HIV drugs safely for decades. However, some people do change treatment because of side-effects, so your healthcare team will be used to discussing these sorts of problems and looking at alternative drug choices.

Remember, if you experience any side-effects, mention them at your clinic. If a side-effect persists, it's nearly always possible to do something about it.

You can find out more about the guidelines for HIV treatment for adults in our summaries of the 2012 guidelines, produced by NAM for BHIVA: www.aidsmap.com/UK-treatment-guidelines.

Recommended first HIV treatment combination

When you discuss starting HIV treatment with your healthcare team, they will talk to you about the known side-effects of each drug. Make sure you tell them about any concerns you have; they should take these into account in helping you choose the most suitable

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treatment combination for you.

If you are starting HIV treatment for the first time, the recommended treatment is a combination tablet (currently known as *Truvada*), which contains two drugs:

- tenofovir, a nucleotide reverse transcriptase inhibitor (NtRTI)

and

FTC (emtricitabine), a nucleoside reverse transcriptase inhibitor (NRTI)

taken with one of the following drugs as a third drug in the combination:

- atazanavir (*Reyataz*), boosted with ritonavir. This is a drug from the protease inhibitor

class. It has its anti-HIV effect boosted by taking it with a small dose of a second protease inhibitor called ritonavir.

or

- darunavir (*Prezista*), boosted with ritonavir. Darunavir is also a protease inhibitor.

or

- efavirenz (*Sustiva*). This is a non-nucleoside reverse transcriptase inhibitor (NNRTI).

or

- raltegravir (*Isentress*). This is an integrase inhibitor.

Tenofovir, FTC and efavirenz are also available in a fixed-dose combination tablet called *Atripla*.

You can find out more about these drugs in the NAM booklet, *Anti-HIV drugs*.

HIV treatment combinations and their side-effects

Although these drugs are very effective and generally safe, they can still cause side-effects. Details of these are provided below. You can find more information on the most common side-effects on pages 40 to 48.

***Truvada* (FTC and tenofovir)**

Both drugs in *Truvada* are usually well tolerated. But they can cause diarrhoea, nausea (feeling sick) and vomiting (being sick). See pages 40 to 43 for more information on dealing with these. Other very common or common side-effects of both are headache, stomach pain, dizziness, rash and a feeling of weakness.

Other common side-effects of FTC include insomnia and abnormal dreams, neutropenia

(lowered white blood cells), raised liver and pancreatic enzymes, raised creatine kinase levels, heartburn, raised blood sugar and triglycerides (blood fats), and an allergic reaction. FTC can cause changes in the colour of the skin (known as hyperbilirubinaemia), particularly in people of non-white race. You should talk to your doctor if this happens to discuss your treatment options.

Other common side-effects of tenofovir include flatulence, low blood phosphate levels, increased transaminases, tiredness and bloating.

Kidney problems can be a rare side-effect of tenofovir, particularly for people who are taking other medicines that affect the kidneys,

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or for those who have other risk factors for kidney disease, such as high blood pressure or diabetes. Your regular HIV monitoring will include tests to check the health of your kidneys.

More rarely, there is a long-term risk of developing bone problems as a result of treatment with tenofovir. Your regular HIV monitoring will include blood tests to check levels of minerals to make sure that you are not at risk of this side-effect.

Uncommon side-effect of FTC: Anaemia.

Like other NRTIs, rarely, tenofovir can cause lactic acidosis.

Atazanavir (Reyataz)

Generally, people tolerate atazanavir well.

Very common or common side-effects: Nausea, diarrhoea, rash, stomach ache, headache, insomnia, vomiting, heartburn, tiredness, lipodystrophy, diabetes.

A common side-effect of atazanavir is hyperbilirubinaemia, or raised bilirubin levels. Bilirubin is a waste product produced by the liver during the breakdown of old red blood cells. If levels of bilirubin increase this can cause jaundice - yellowing of the skin and whites of the eyes. This is not dangerous, but some people find it distressing.

Talk to your doctor at your routine HIV clinic

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appointment if you notice a yellowing of your skin or eyes. However, if there is yellowing, and you also feel sick, vomit, have diarrhoea, have stomach pain, or feel generally unwell, you should see a doctor immediately. These could be signs of liver inflammation (hepatitis), which needs immediate monitoring and treatment.

Uncommon or rare side-effects: Kidney stones, gallstones, abnormal liver function, changes in heart rhythm. If you have an existing heart condition, or are on other treatments that can affect heart function, your heart function will be regularly monitored. Rarely, atazanavir can cause a hypersensitivity (allergic) reaction, including a severe rash called Stevens Johnson syndrome. If you develop a rash with other symptoms, such as a fever, seek medical advice.

See page 38 for more information and advice.

Atazanavir is not recommended for people with reduced kidney function who need dialysis. Your doctor will test your kidney function before prescribing it, but it is important to tell them about any kidney problems you have or have had in the past.

Unlike some other anti-HIV drugs, atazanavir is less likely to increase lipid (blood fat) levels, so may be a good option for people with high cholesterol or other risk factors for heart disease.

Darunavir (*Prezista*)

Generally, people tolerate darunavir well.

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Very common or common side-effects:

Diarrhoea, vomiting, nausea, stomach ache, increased blood amylase, heartburn, bloating, headache, peripheral neuropathy, dizziness, insomnia, lipodystrophy, raised liver and pancreatic enzymes, a feeling of loss of strength, tiredness, rash. A rash is more likely if it is taken in combination with raltegravir.

Uncommon side-effects, rare or very rare side-effects: Abnormal liver function, abnormal kidney function, changes in heart rhythm. Rarely, darunavir can cause a hypersensitivity (allergic) reaction, including a severe rash called Stevens Johnson syndrome. If you develop a rash with other symptoms, such as a fever, seek medical advice. See page 38 for more information and advice.

Side-effects seem to be less common and less severe in people who take darunavir once a day compared to twice-daily dosing.

Efavirenz (Sustiva)

Many people have side-effects in the first few weeks of taking efavirenz, but these often go away fairly quickly.

Very common or common side-effects: Rash, dizziness, headache, diarrhoea, nausea, vomiting, tiredness, stomach ache, raised triglycerides (blood fats), raised liver enzymes.

Efavirenz can cause a feeling of being 'out of sorts', confusion, impaired concentration, sleep disturbance, abnormal dreams. Mental health problems including depression, anxiety

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and low mood have also been reported as side-effects of efavirenz.

These side-effects are often most noticeable in the first few weeks after treatment with efavirenz is started and then lessen or even go away completely. However, a small number of people experience longer-term or more serious sleep and mood problems due to treatment with efavirenz and some people need to stop taking the drug because of these.

If you do experience side-effects caused by efavirenz, discuss these with your doctor. There may be a number of options available to you to help reduce these side-effects. One simple step you can take is to avoid taking efavirenz with a high-fat meal as this will

increase the level of the drug in your body and can increase the side-effects. You could do this by taking it on an empty stomach or at least two hours after food. Taking it an hour or so before bed means that the drug level should be highest while you are asleep.

If you have a history of mental health problems, efavirenz might not be a good choice and you may want to talk about other treatment options with your doctor.

Uncommon side-effects: Liver problems, pancreatitis. An uncommon side-effect of efavirenz is a hypersensitivity (allergic) reaction, including a severe rash called Stevens Johnson syndrome. If you develop a rash with other symptoms, such as a fever, seek medical

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advice. See page 38 for more information and advice.

Rarely, people experience serious mental health problems such as psychosis or delusions; this seems to be more likely if you have had mental health issues in the past. If you are worried about your mood or behaviour, bear in mind changes in these could be linked to efavirenz. Talk to your doctor about your concerns.

Raltegravir (Isentress)

Generally, people tolerate raltegravir well.

Very common and common side-effects:
Decreased appetite, headache, insomnia, abnormal dreams, dizziness, vertigo, bloating,

stomach ache, flatulence, nausea, vomiting, diarrhoea, rash, muscle weakness, tiredness, fever, raised liver and pancreatic enzymes, raised blood fats.

Uncommon side-effects: Extreme thirst (polydipsia).

In uncommon cases, raltegravir has been known to cause a hypersensitivity (allergic) reaction, including a severe rash called Stevens Johnson syndrome. If you develop a rash with other symptoms, such as a fever, seek medical advice. See page 38 for more information and advice.

Unlike some other anti-HIV drugs, raltegravir is less likely to increase lipid (blood fat) levels,

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so may be a good option for people with high cholesterol or other risk factors for heart disease.

Other options if you are starting treatment

Your doctor may suggest you start treatment on a different drug combination to the ones described above.

There may be reasons why one of the combinations recommended for starting HIV treatment is not suitable for you. This could be because of possible interactions with other drugs you are taking, or because the type of HIV you have is resistant to one or more drugs. Or it could be because you want to avoid certain side-effects.

In some cases, if your doctor thinks it will work

as well for you, they may suggest you start on a combination that costs less for the NHS to buy. Your doctor will only do this if they also think this combination will work for you.

There are some alternative combinations recommended for people starting HIV treatment.

An alternative to *Truvada* is the combination drug *Kivexa* (3TC and abacavir).

Alternative choices for a third drug in the combination are:

- *Kaletra*, the protease inhibitor lopinavir, boosted with ritonavir, taken in two pills containing the combined drugs

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or

- nevirapine (*Viramune*, *Viramune prolonged-release*), a drug in the NNRTI class

or

- rilpivirine (*Edurant*). This is the latest drug in the NNRTI class

or

- fosamprenavir (*Telzir*), also a protease inhibitor that needs to be boosted with ritonavir.

Truvada and rilpivirine are also available in a fixed-dose combination tablet called *Eviplera*.

You can find out more about these drugs in the NAM booklet, *Anti-HIV drugs*.

Although these drugs are effective and generally safe, they can still cause side-effects.

Details of these are provided below. You can find more information on the most common side-effects on pages 40 to 48.

***Kivexa* (3TC and abacavir)**

Generally, people tolerate *Kivexa* well.

Very rarely, abacavir can cause a hypersensitivity (allergic) reaction, including a severe rash called Stevens Johnson syndrome. If you develop a rash with other symptoms, such as a fever, seek medical advice. See page 36 for more information and advice.

Some (but not all) research has linked abacavir to an increased risk of heart attack, particularly for people who have other risk factors for heart disease. Because of this, abacavir is

HIV treatment combinations and their side-effects

not recommended for people who have risk factors for heart disease, if a suitable alternative is available.

Both abacavir and 3TC can cause rash, fever, tiredness, headache, nausea, vomiting and diarrhoea. These side-effects are usually quite mild and lessen or go away completely after a few weeks of treatment. Your doctor can also give you other medicines to control some of these side-effects if you need them. See pages 40 to 48 for more information on how to manage these.

Other very common or common side-effects of 3TC include cough, nasal symptoms, stomach ache, hair loss, insomnia and joint pain.

Another common side-effect of abacavir is loss of appetite.

Rare side-effects of 3TC: Liver damage (hepatitis). Very rarely pancreatitis.

Like other NRTIs, rarely, abacavir and 3TC cause lactic acidosis.

Kaletra (lopinavir/ritonavir)

Very common or common side-effects:

Respiratory tract infections (infections of the sinuses, throat, airways or lungs), skin infections, diabetes, swollen glands, anaemia and other blood changes, anxiety, dizziness, insomnia, headache, nausea, vomiting, diarrhoea, stomach ache and bloating, tiredness, weakness, muscle pain, heartburn,

HIV treatment combinations and their side-effects

rash, raised liver enzymes and liver toxicity, lipodystrophy, erectile dysfunction, menstrual changes (heavy periods or missing periods).

Kaletra is not recommended for people with increased risk for heart disease as it can cause increases in lipids (blood fats) and high blood pressure. Your regular HIV monitoring will include tests to measure levels of blood fats (cholesterol and triglycerides). See page 51 for more information on managing this sort of side-effect.

Kaletra can cause pancreatitis. This nearly always occurs in people who have had it before, or who are on other medication that can cause pancreatitis.

Rare side-effects: Changes in heart rhythm.

Nevirapine (*Viramune, Viramune prolonged-release*)

To reduce the risk of an allergic reaction to nevirapine, you should not start treatment with nevirapine if you have a detectable viral load and, for men, a CD4 cell count above 400 or, for women, a CD4 cell count of more than 250. If you have an undetectable viral load, you can start treatment with nevirapine but your liver function will be carefully monitored.

The main side-effect of nevirapine is rash. To reduce the risk of this, for the first two weeks of treatment the dose of nevirapine is 200mg once daily, after which it is increased to 200mg twice daily. Nevirapine prolonged-release is taken as a 400mg dose once a day after the first two weeks of treatment.

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For most people, the rash is not serious, and clears up. A small number of people need to change treatment because of the rash the nevirapine can cause, and a very small number of people require hospitalisation because of this rash.

Other very common or common side-effects include headache, nausea, vomiting, stomach ache, diarrhoea, fever, tiredness, raised liver enzymes. Nevirapine can cause serious liver toxicity. See page 37 for more information and advice.

Other uncommon or rare side-effects: Raised blood pressure, anaemia. Uncommonly, nevirapine can cause a severe rash called Stevens Johnson syndrome. If you develop a rash with other symptoms, such as a fever,

seek medical advice. See page 37 for more information and advice.

Rilpivirine (*Edurant*, also available in the combination drug *Eviplera*)

Generally, people tolerate rilpivirine well. It's important it's taken with food.

Very common or common side-effects: Insomnia, tiredness, drowsiness, headache, nausea, rash, changes in liver and pancreas function, changes in blood counts, increases in blood fats (cholesterol and triglycerides), lack of appetite, depression, dizziness, stomach ache, vomiting, dry mouth.

Rare side-effects: At doses above 25mg, changes in heart rhythm (known as QT prolongation).

HIV treatment combinations and their side-effects

Fosamprenavir (Telzir)

Very common or common side-effects: Nausea, vomiting, diarrhoea, rash, abdominal pain, headache, dizziness, tiredness, tingling around the mouth, raised liver and pancreas enzymes, lipodystrophy, diabetes.

Fosamprenavir is not recommended for people with increased risk for heart disease as it can cause increases in lipids (blood fats). Your regular HIV monitoring will include tests to measure levels of blood fats (cholesterol and triglycerides). See page 51 for more information on managing this sort of side-effect.

Rarely, fosamprenavir can cause a severe rash called Stevens Johnson syndrome. If you

develop a rash with other symptoms, such as a fever, seek medical advice. See page 38 for more information and advice.

Drugs not recommended for first-line HIV treatment

Some drugs are no longer recommended for standard HIV treatment in the UK. These include d4T (stavudine, *Zerit*) and ddI (didanosine, *Videx*), because of the serious and long-term side-effects they can cause, such as peripheral neuropathy and fat loss or gain (lipodystrophy). There is more information on these later in this booklet.

Other drugs are no longer recommended for people starting HIV treatment or changing to a new treatment, although there may be people

HIV treatment combinations and their side-effects

who are already on these drugs and happy to continue with them. These include the protease inhibitor saquinavir (*Invirase*).

HIV treatment during pregnancy

If you have conceived when already on treatment, you can usually stay on your current combination of drugs, if these are successfully suppressing your viral load. If you are pregnant and need treatment for your own health, you should start on one of the combinations recommended in the British HIV Association (BHIVA) treatment guidelines for adults (see page 17).

Many pregnant women have morning sickness – nausea (feeling sick) and vomiting (being sick) – in the first three months of pregnancy. If

you are less than 12 weeks pregnant, and your CD4 count is around 350, you and your doctor could discuss waiting to start HIV treatment until morning sickness stops (usually at about 13 to 14 weeks). This is because some anti-HIV drugs can also make you feel sick during the first few weeks of treatment.

Otherwise, you should start HIV treatment by week 24 of your pregnancy, at the latest. The combination used will depend on a range of factors.

AZT (zidovudine, *Retrovir*) is not recommended for people starting treatment for their own health, but is still sometimes used as a short-term treatment to prevent mother-to-child transmission during pregnancy and

HIV treatment combinations and their side-effects

birth. This is because there is good evidence that AZT is a safe and effective drug to use in preventing mother-to-child transmission.

Although AZT is the only drug licensed for use during pregnancy, it is now known that other drug combinations are effective in preventing mother-to-child transmission. So your treatment combination may or may not include AZT.

You can find out more about HIV treatment during pregnancy in the booklet in this series, *HIV & women* and you can get personalised information using our online tool *HIV & pregnancy*: www.aidsmap.com/pregnancy. You can find out more about the guidelines for HIV treatment during pregnancy in our

summaries of the 2012 guidelines, produced by NAM for BHIVA: www.aidsmap.com/UK-treatment-guidelines

AZT (zidovudine, *Retrovir*)

Very common and common side-effects: Nausea, vomiting, tiredness, headache, dizziness, stomach ache, muscle pain, feeling unwell, changes in blood counts, raised liver enzymes.

Rare side-effects: Liver toxicity, lipoatrophy (see page 54), lactic acidosis.

Changing treatment because of side-effects

In some circumstances you may need or want to change treatment because of side-effects. This is more likely to be an option if you have little or no resistance to anti-HIV drugs and

HIV treatment combinations and their side-effects

your viral load is undetectable. Then you should be able to stop the drug that is causing your side-effect and switch to a different treatment.

Changing treatment can be more complex if you have a detectable viral load or you have HIV that is resistant to some anti-HIV drugs. Your doctor will look at the results of resistance tests and discuss possible treatment options with you. Having resistance will, however, limit the number of replacement drugs that are available to you.

It also makes good sense to ask about the possible side-effects of the drugs you are considering switching to.

Treatment for people who have taken a lot of anti-HIV drugs in the past

A number of anti-HIV drugs are now available that provide very important treatment options for people who have taken a lot of HIV treatment in the past, particularly those with drug-resistant virus.

These drugs are particularly effective against HIV because they work against the virus in a slightly different way to the older anti-HIV drugs, or work against virus resistant to other drugs in the same drug class. These drugs are:

- T-20 (enfuvirtide, *Fuzeon*)
- maraviroc (*Celsentri*)
- raltegravir (*Isentress*, also used by people starting treatment for the first time)

HIV treatment combinations and their side-effects

- etravirine (*Intelence*)
- tipranavir (*Aptivus*).

T-20 (enfuvirtide, *Fuzeon*)

This is currently the only anti-HIV drug that is given by injection, and is now only prescribed in very rare and specific situations. The key side-effects are pain and a hardening of the skin at the site of the injection. These are often called injection-site reactions. If you need to take T-20, you'll be given information about how to inject it and how to reduce the risk of injection-site reactions developing.

Other very common or common side-effects include infections such as sinusitis, flu and pneumonia, decreased appetite, peripheral neuropathy (see page 56) and pancreatitis.

T-20 has some rarer side-effects as well, including a hypersensitivity reaction. Your doctor should explain these side-effects to you, and what action to take, before you start treatment with it.

Maraviroc (*Celsentri*)

Generally, people tolerate maraviroc well.

Very common and common side-effects: Nausea, diarrhoea, tiredness, headache, depression, insomnia, loss of appetite, stomach ache, rash, raised liver enzymes, weakness, anaemia.

Uncommon, rare and very rare side-effects: Liver problems, kidney problems, angina, cancers.

HIV treatment combinations and their side-effects

Rarely, maraviroc can cause a severe rash called Stevens Johnson syndrome, and very rarely serious liver toxicity. If you develop a rash with other symptoms, such as a fever, seek medical advice. See page 38 for more information and advice.

If you also have hepatitis B or hepatitis C, or have any other liver problems, your doctor should monitor you carefully and do blood tests to check the health of your liver.

Raltegravir (Isentress)

See page 24.

Etravirine (Intence)

Generally, people tolerate etravirine well.

Very common or common side-effects: Rash, diarrhoea, headache, nausea, vomiting, reflux, stomach ache, anxiety, night sweats, insomnia, tiredness, raised lipids (cholesterol and triglycerides), diabetes, changes to blood counts, high blood pressure, peripheral neuropathy (see page 56), kidney failure, heart attack.

Uncommon, rare and very rare side-effects: Liver problems, pancreatitis.

There is a risk of developing a hypersensitivity (allergic) reaction in the form of a severe rash (Stevens Johnson syndrome). See page 38 for more information on this.

Hypersensitivity (allergic) reactions

Tipranavir (*Aptivus*)

This drug is now very rarely used.

Very common and common side-effects:

Nausea, diarrhoea, vomiting, bloating, stomach ache, heartburn, tiredness, headache, raised lipids (cholesterol and triglycerides), flatulence, rash.

Rare side-effects: Bleeding in brain, liver toxicity, peripheral neuropathy (see page 56), pancreatitis.

Hypersensitivity (allergic) reactions

The anti-HIV drugs with the greatest risk of hypersensitivity, or allergy, are abacavir (*Ziagen*, also in the combination pills *Kivexa* and *Trizivir*) and nevirapine (*Viramune*). Atazanavir (*Reyataz*), etravirine (*Intelence*), efavirenz (*Sustiva*, also in *Atripla*), darunavir (*Prezista*), fosamprenavir (*Telzir*), maraviroc (*Celsentri*) and raltegravir (*Isentress*) may also cause an allergic reaction.

Abacavir hypersensitivity

Abacavir can cause a serious hypersensitivity (allergic) reaction. This is associated with the presence of a particular gene called HLA-B*5701. Before starting treatment with

Hypersensitivity (allergic) reactions

abacavir (or any treatment that contains abacavir) you should first have a blood test to see if you have this gene. If the test is positive you **must not** take abacavir. If the test is negative, it is highly unlikely that an allergic reaction will occur, but contact your HIV clinic immediately (or A&E if out of hours) if you begin to feel unwell after starting the drug.

In the box with the drug there is an 'alert card', which you should carry with you for the first six weeks of taking abacavir. The particular side-effects you should look out for during this time are:

- Any skin rash **OR**
- If you get one or more symptoms from at least TWO of the following groups:

Group 1: fever

Group 2: shortness of breath or sore throat or cough

Group 3: nausea or vomiting or diarrhoea or abdominal pain

Group 4: severe tiredness or achiness or generally feeling ill.

You should never retry abacavir, or take *Trizivir* or *Kivexa*, if you have had an allergic reaction to abacavir previously.

Nevirapine liver toxicity

A small number of people who start treatment with nevirapine (*Viramune*) develop serious liver problems. This can cause very serious skin rashes (including Stevens Johnson syndrome or toxic epidermal necrolysis). Symptoms can include:

Hypersensitivity (allergic) reactions

- fever
- generally feeling ill
- extreme tiredness
- muscle or joint aches
- blisters
- oral lesions
- eye inflammation
- facial swelling
- signs and symptoms of liver problems (e.g., yellowing of your skin or whites of your eyes, dark or tea-coloured urine, pale-coloured stools/bowel movements, nausea, vomiting, loss of appetite, or pain, aching or sensitivity on your right side below your ribs).

If you develop these symptoms whilst taking this drug, you should contact your HIV clinic immediately (or A&E if out of hours).

Your liver function will be monitored closely during the first 18 weeks you are on nevirapine.

To reduce the risk of an allergic reaction to nevirapine, you should not start treatment with nevirapine if you have a detectable viral load and, for men, a CD4 cell count above 400 or, for women, a CD4 cell count of more than 250.

If you have an allergic reaction of this type to nevirapine, you should not take it again in the future.

Other hypersensitivity reactions

A very rare hypersensitivity (allergic) reaction has been reported in some people using other anti-HIV drugs, including atazanavir, etravirine, efavirenz, darunavir, fosamprenavir, maraviroc

Hypersensitivity (allergic) reactions

and raltegravir. This can cause a severe rash, called Stevens Johnson syndrome. See your HIV clinic immediately (or A&E if out of hours) if you develop a rash together with any of these symptoms:

- fever
- feeling generally unwell or extremely tired
- muscle or joint ache
- blistering of the skin
- mouth ulcers
- swelling of the eye, lips, mouth or face
- breathing difficulties
- yellowing of the skin or eyes
- dark urine
- pale stools
- pain, aching or sensitivity on the right-hand side of the body, below the ribs.

If you have this sort of reaction, you should not take the drug which caused it again in the future.

It's possible that other drugs, including other anti-HIV drugs, might rarely cause allergic reactions too. It is therefore important that you tell your doctor as soon as possible if you develop a rash, fever, or feel generally unwell soon after starting treatment with a new drug.

Common side-effects

This section of the booklet provides some more information on the commonest side-effects that the anti-HIV drugs currently in use can cause.

It is intended to provide you with information to help you recognise a side-effect should you develop one. There's also information on what you can do to help control side-effects.

Key things to remember about side-effects:

- Many symptoms, for example headaches, diarrhoea, feeling or being sick and rashes can have causes other than anti-HIV drugs. If you develop such a symptom, HIV treatment might not be the cause.

- Mention suspected side-effects to your doctor. It is important to find out the cause of symptoms you are experiencing.
- You do not have to put up with side-effects – there is nearly always something that can be done about them.

Diarrhoea

Diarrhoea is a possible side-effect of most anti-HIV drugs.

With some drugs, diarrhoea goes away after the first few weeks or months of treatment. However, for some people it becomes a permanent feature of taking a particular drug. Try to avoid coffee, raw vegetables and spicy food as they can make diarrhoea worse.

Common side-effects

Changes in diet have little effect on drug-related diarrhoea. However a variety of treatments are available which can help control diarrhoea, particularly the anti-diarrhoea medicine loperamide (sometimes known by its trade name *Imodium*). Your doctor should give you a prescription for this if you start any HIV treatment that can cause diarrhoea, or you can buy it over the counter at a pharmacy. Stronger anti-diarrhoea drugs, such as lomotil or octreotide, can be prescribed by your doctor.

It is important that you continue to eat and drink even if you have diarrhoea caused by your medication. Diarrhoea can cause you to lose large amounts of salts and water from your body, so it is important to drink plenty of fluids. Rehydration drinks (for example, *Diarolyte*)

can help replace sugars and salts as well as providing extra fluids. You can buy these at a chemist or supermarket.

Eating foods like bananas, potatoes, chicken or fish will help you replace potassium, levels of which are commonly reduced in people with severe diarrhoea. Soluble fibre from natural sources like white rice, white pasta, pulses, oats, bananas, apples and pears can help reduce diarrhoea.

In many cases, avoiding foods that are high in fat, bulky (insoluble) fibre (such as whole grains, nuts and seeds), or lactose (found in dairy products such as cow's milk and cheese) may help reduce the symptoms of diarrhoea.

Common side-effects

If you are losing weight because of diarrhoea, it is important to speak to a dietitian as soon as possible who will work with you to develop a diet which is more appetising, or easy to absorb.

Diarrhoea can have other causes. If you have diarrhoea for more than a few days, especially if you feel unwell, you should see your doctor. They may suggest you have a stool sample checked for infections.

Increasing or decreasing the fibre content of your diet may help if you have irritable bowel syndrome, as might anti-spasmodic therapies such as *Colofac*.

Feeling or being sick

Feeling sick (nausea) or being sick (vomiting) are possible side-effects of most anti-HIV drugs. Your doctor may give you pills (called anti-emetics) to stop you being sick if you are starting an anti-HIV drug that has nausea and vomiting as a possible side-effect. Taking these about 30 minutes before you take your anti-HIV drugs can help prevent these symptoms.

As with many other possible side-effects, nausea and vomiting tend to be worst in the first few weeks after you start treatment and then often lessen or go away completely.

Nausea and vomiting can have other causes, so your HIV treatment might not be the cause. It makes good sense to tell your HIV doctor if you

Common side-effects

are feeling sick or being sick, particularly if you have other symptoms as well, especially a fever.

Whatever the cause, do not feel obliged to just put up with it – nausea and vomiting can prevent you from getting enough food and nutrients and from sticking with your HIV treatment. As well as asking your doctor about anti-sickness medication, the following practical tips may be helpful and can be discussed with your doctor, pharmacist or a dietitian:

- Eat small, frequent meals throughout the day rather than two or three large meals.
- Don't eat liquid and solid food at the same meal. Space them at least one hour apart.
- Avoid eating greasy, fatty, fried or spicy food. Instead, choose bland food.
- Try dry food such as toast, crackers, cereal, and fruit and vegetables that are bland or soft.
- Salty food such as crackers, pretzels and popcorn can help reduce nausea. Carry a packet with you when you leave the house.
- Don't lie flat for at least an hour after you eat.
- Eat food cold or at room temperature – hot food can worsen nausea.
- Herbal tea (e.g. peppermint or chamomile) or root ginger can help settle upset stomachs.

Common side-effects

Headache

Headache is a possible side-effect of many anti-HIV drugs. In most cases, these are mild and lessen or go away completely after a few weeks of treatment with the drug. Pain killers such as paracetamol can provide relief.

It makes good sense to tell your doctor about headaches, particularly if they are severe or last more than a few days.

Mood and sleep problems

Efavirenz (*Sustiva*, also in the combination pill, *Atripla*), can cause a number of mood and sleep problems, including anxiety and depression, feeling spaced out during the day or having vivid dreams at night. Rilpivirine (*Edurant*) can also cause mood changes and depression.

When these side-effects occur, they are normally mild and lessen or go away after a few weeks of treatment. But for some people they are not tolerable and they need to change treatment because of them. Tell your doctor if you are experiencing these side-effects. If you have a history of mental health problems, these drugs may not a good choice for you.

Some people find that taking efavirenz just before going to bed helps them to feel better during the day. A short course of sleeping tablets may also help to re-establish your sleep patterns.

You can find out more about managing mood changes, anxiety and depression, and looking after your emotional wellbeing, in the booklet in this series *HIV, mental health & emotional wellbeing*.

Common side-effects

Rash

Rash can be a side-effect of a number of anti-HIV drugs.

Such rashes often lessen or go away after a few weeks of treatment. Even so it is a good idea to report rashes to your doctor. A rash can also be a sign of an infection. Some rashes can indicate the presence of serious side-effects. This is particularly important if you are taking abacavir, etravirine, maraviroc, nevirapine or raltegravir, where there is a possibility of a serious hypersensitivity (allergic) reaction. See page 39 for more information on what symptoms to look out for. It's important you take fast action if you think you are suffering from this sort of reaction.

People starting HIV treatment with nevirapine will take a 14-day reduced lead-in dose (200mg) of immediate-release nevirapine in order to reduce the risk of rash, a common side-effect during the first few weeks of nevirapine treatment. Treatment with *Viramune prolonged-release* should not begin until the rash has gone away. Always tell your doctor about any rash you develop while taking nevirapine. If a rash persists for more than one month, or becomes more severe, a different drug should be used.

Sexual problems

Sexual problems (sometimes called sexual dysfunction) are common in people with HIV. They are sometimes thought of as a side-effect of HIV treatment, but can have a number of

Common side-effects

possible causes, so it's often difficult to say if HIV treatment is the cause.

Sexual problems can include a loss of interest in sex, or reduced sexual performance (for example, delayed orgasm or an inability to achieve and maintain an erection).

As well as treatment side-effects (not only of HIV drugs but of commonly used medicines like antidepressants as well), possible causes also include anxiety and stress, mental health problems such as depression, drug and alcohol use, illness, and ageing.

More is known about sexual problems in men with HIV than women with HIV. Protease inhibitors are the type of anti-HIV drug most

associated with sexual problems in men – normally problems achieving or maintaining an erection.

The extent to which protease inhibitors cause erectile problems is far from certain, and it's not inevitable that you'll develop such problems if you start treatment with a protease inhibitor.

If you do develop sexual problems it's good to know that there's a lot that can be done about them so it makes good sense to mention them to a member of your healthcare team.

There could be other medical causes for your sexual problems, so your doctor may do tests to monitor your testosterone level or check the health of your heart and arteries.

Common side-effects

It's important to consider if there are any psychological issues that could be contributing to your sexual problems.

Medicines are available to treat erectile dysfunction in men. These are called tadalafil (*Cialis*), vardenafil (*Levitra*) and sildenafil (*Viagra*). They work by increasing the flow of blood to the penis. Your doctor may be able to provide you with an NHS prescription for these drugs, or it may be possible to have them prescribed privately.

All three of these drugs can interact with anti-HIV drugs, particularly protease inhibitors and NNRTIs. If you are taking HIV treatment, your prescribed dose of an erectile dysfunction drug will be reduced to half the standard dose. Tell your HIV doctor or pharmacist about other

medicines you are taking as some can interact with erectile dysfunction drugs.

You shouldn't use poppers if you are taking erectile dysfunction drugs as this can cause a potentially dangerous drop in blood pressure.

You can find out more about dealing with sexual problems in NAM's booklet *HIV & sex*.

Tiredness

Tiredness (fatigue) is a possible side-effect of most anti-HIV drugs.

As with most other side-effects, the risk of fatigue is greatest in the first few weeks after you start treatment with a drug, and then it is likely to lessen or go away completely.

Longer-term side-effects

It makes good sense to tell your doctor if fatigue is a problem for you. If the cause is your HIV treatment there is a good chance that something can be done about it. Fatigue can have other causes as well, so tell your doctor about prolonged tiredness so he or she can investigate possible causes.

Getting enough sleep, eating a good balanced diet, and regular exercise can also help with fatigue.

Longer-term side-effects

Kidney problems

Effective HIV treatment has significantly reduced the risk of serious kidney disease in people with HIV. However, most anti-HIV drugs can cause some damage to the kidneys, so your routine HIV care will involve regular tests to check on the health of your kidneys.

Tenofovir (*Viread*, also in the combination pills *Truvada*, *Atripla* and *Eviplera*) is processed by the body through the kidneys, and there is evidence that it can cause damage to the kidneys over time. UK treatment guidelines recommend that people with moderate or severe existing kidney disease should not

Longer-term side-effects

take tenofovir if there is a suitable alternative. People with other risk factors for kidney disease (for example high blood pressure or diabetes) might have an increased risk of developing kidney problems when taking this drug.

If you develop kidney problems, it might be necessary to change your HIV treatment or to have additional treatment for this.

Metabolic changes

Anti-HIV drugs can disrupt your metabolism – the way your body processes the substances it needs to work properly.

Specifically, anti-HIV drugs can cause abnormal levels of lipids – blood fats, or cholesterol and triglycerides – and also blood sugar.

Cholesterol

There are two types of cholesterol: high-density lipoprotein or HDL cholesterol, often called 'good' cholesterol, and low-density lipoprotein (LDL), or 'bad', cholesterol.

Levels of HDL cholesterol are often reduced in people with HIV and other chronic illnesses. High levels of LDL cholesterol indicate that you are at greater risk of heart disease, and increases of LDL cholesterol are often seen in people taking anti-HIV drugs.

High rates of LDL cholesterol can cause narrowing and hardening of the arteries, increasing the risk of heart disease, heart attack and stroke. If you have high LDL cholesterol, the following factors increase your risk of heart disease even further:

Longer-term side-effects

- Smoking.
- High blood pressure.
- A family history of heart disease.
- Being physically unfit.
- Being aged over 45 for men and over 55 for women.
- Diabetes or insulin resistance.
- High blood sugars.
- Being very overweight, particularly with a lot of fat around the waist.
- Use of stimulant recreational drugs such as cocaine or amphetamines.

It is particularly important to monitor LDL cholesterol levels if you are taking a protease inhibitor.

Triglycerides

Triglycerides are fatty acids derived from fat, sugar and starches in food. These travel through the bloodstream and are stored in tissues or in the liver. Levels of triglycerides can be increased by some anti-HIV drugs.

Glucose

Glucose is a form of sugar found in the blood. High levels of glucose can increase the risk of heart disease. Levels of glucose can be increased by some anti-HIV drugs.

Insulin is the substance produced by the body to control glucose levels in the blood. Some people taking anti-HIV drugs need to produce more insulin to keep their blood levels of glucose normal. This is called insulin resistance.

Longer-term side-effects

You will have your blood glucose checked as part of your regular HIV monitoring.

Symptoms of metabolic change

Abnormal levels of fats and sugars in the blood can sometimes cause symptoms including:

- Tiredness.
- Dizziness (due to high blood pressure).
- Loss of concentration.
- More frequent urination.
- Thirst.

However, some people don't notice any symptoms, even when they've had abnormal levels of fats and sugars for a long time and are at greater risk of heart disease.

Heart disease and anti-HIV drugs

Levels of fats in your blood may start to rise when you start HIV treatment, particularly if you are taking certain protease inhibitors. Sometimes the size of the increase will mean you'll need to take some action to reduce it. This will probably start with making changes to your diet and doing more exercise, but might also involve taking medication to control blood fats. You can find out more about how to change your diet in NAM's booklet *Nutrition*.

Large studies of people taking protease inhibitors have shown that they have a slight, but nevertheless significant, increase in their risk of heart disease. Some (but not all) studies have also suggested that abacavir (*Ziagen*, also in the combination pills *Kivexa* and *Trizivir*)

Longer-term side-effects

might increase the risk of heart disease, particularly for people who already have risk factors for heart problems.

If you have any existing risk factors for heart disease, your HIV treatment should be carefully chosen to ensure that it doesn't raise the risk even further. And a 'risk' of heart disease does not automatically mean that heart problems will develop. A lot can be done to prevent this happening.

Your cholesterol, triglyceride and glucose levels should be monitored each time you have a routine clinic visit. This will mean that your doctor can spot any warning signs early.

There is also a lot you can do to reduce the risk of developing heart disease. This includes eating a healthy diet, with lots of fresh fruit and vegetables and without too much fat, taking regular exercise, and not smoking.

You can find out more about eating well, managing metabolic changes and taking exercise in NAM's booklet *Nutrition*.

In some circumstances your doctor might prescribe what are called lipid-lowering drugs. These are used to reduce the risk of heart disease and prevent existing heart disease from getting worse. They include statins (to lower cholesterol) and fibrates (to lower triglycerides and also cholesterol). Some statins can interact with protease inhibitors,

Longer-term side-effects

and both statins and fibrates can cause their own side-effects, so your doctor will monitor you to see if these are developing.

Liver problems

Having a healthy liver is important for people with HIV as most anti-HIV drugs are processed by the liver. Some people have experienced liver problems when taking HIV treatment. In many cases, they had other risk factors, such as also having hepatitis B or C, having an opportunistic infection or being treated with other medicines that can harm the liver.

Having a low CD4 cell count when starting HIV treatment, especially if you have also had an opportunistic infection, and the treatment for some of those infections, can cause liver

problems. And some aspects of your lifestyle can affect the health of your liver, such as drinking heavily or using recreational drugs. Your HIV clinic will be able to offer advice and support if you are worried about your alcohol or drug use.

Your routine HIV care will involve blood tests to monitor the health of your liver. If you do develop liver problems, possible options include changing your HIV treatment or having additional treatment for your liver problems.

Changes in your diet may also help, so try to eat lots of fresh fruit and vegetables, avoid fatty food (as the liver is the organ that breaks down fat in your body), and eat slow-release starchy foods, such as bread and potatoes. NAM's booklet *Nutrition* provides information on eating well.

Longer-term side-effects

Lipodystrophy

Lipodystrophy is a syndrome which causes changes in body shape. It was originally thought that the cause was protease inhibitors, but it now seems that some drugs in the NRTI class may be the main cause. The long-term use of the drugs most associated with lipodystrophy – AZT and d4T – is now avoided as much as possible. Anti-HIV drugs now prescribed in the UK only rarely cause changes in body shape.

Sometimes people find that they gain weight after starting HIV treatment. This weight gain is more likely to be due to improved health as the result of being on treatment, or to the most common reasons people put on weight – eating too much and/or not doing enough

physical exercise. You can find out more about maintaining a healthy weight in NAM's booklet *Nutrition*.

Body fat changes seen in people taking HIV drugs can involve fat loss, fat gain, or a mixture of both. This may result in: increased waist size (without rolls of fat); increased breast size; fat gain around the back of the neck and upper back; fat gain around the neck and jaw; facial wasting, especially of the cheeks; wasting of the buttocks; prominent veins in the arms and legs (because of fat loss). Some people have developed small lumps of fat called lipomas, often in the limbs or trunk.

The abdominal fat gain in lipodystrophy is made up of hard fat that accumulates

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around the internal organs, causing the belly to feel taut and pushed out. This is different to the squeezable fat gained if people put weight on through over-eating or lack of exercise.

Even when people have stopped taking the treatment associated with fat loss, the body fat can be slow to return, and may not come back at all. Fat loss from the face can be repaired in a number of ways. The most commonly used technique involves injections of a product called poly-lactic acid (*New Fill* or *Sculptra*) into the affected areas. This treatment is often available from HIV clinics so ask your doctor or another member of your healthcare team if this treatment is available to you.

Surgery can be an option for removing fat accumulation around the neck, and lipomas can also be surgically removed if needed.

Other possible treatments involve human growth hormone or anabolic steroids. Again, you can talk to your doctor about these.

Diet, regular cardiovascular exercise and weight training have been shown to have some positive effect on fat gain. You can find out more about eating well and the sort of exercise that can help with lipodystrophy in NAM's booklet *Nutrition*.

People who have experienced body fat changes have sometimes found this stigmatising – a visible sign that they are taking HIV treatment.

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The bodily changes can also affect the way that people feel about themselves. If you have developed lipodystrophy and feel this way, acknowledging your feelings and talking to somebody about them can be very helpful. Your HIV clinic should be able to talk to you about accessing talking therapies if you think it would be helpful for you.

Peripheral neuropathy

Nerve damage (neuropathy) can be caused by HIV. It can also be caused by some anti-HIV drugs, and by some treatments for opportunistic infections: some antibiotics, TB drugs, and therapies for Kaposi's sarcoma.

The drugs most closely linked to peripheral neuropathy are d4T and ddI, no longer

routinely used in the UK, and ddC, which is no longer available. Peripheral neuropathy is now a rare side-effect of most anti-HIV drugs. The risk is very small and it is usually dependent on another factor increasing the risk, such as having a CD4 cell count under 100, having had neuropathy before, having another condition that can cause it (such as diabetes), older age or drinking heavily.

Overall, effective HIV treatment reduces the risk of peripheral neuropathy developing.

The nerves which can be damaged by anti-HIV drugs are in the limbs (and very rarely, male genitals), so this side-effect is called peripheral neuropathy.

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Peripheral neuropathy usually involves damage to the nerves in the lower legs and feet or, less commonly, the hands. The symptoms can range from mild tingling and numbness through to excruciating pain that makes it impossible even to wear a pair of socks. Usually both sides of the body are equally affected.

Other symptoms of neuropathy can include dizziness, diarrhoea and sexual dysfunction in men (inability to obtain or sustain an erection).

If you do develop drug-related neuropathy, it is important to discuss this with your doctor. It may be necessary to stop taking the anti-HIV drugs that are contributing to the neuropathy. Once the drug has been stopped, the neuropathy may continue to get worse

for a couple of weeks, but it will often go away over time. If you have been on the treatment for a long time, there may be some permanent nerve damage.

In the meantime, standard painkillers will help with mild pain. If these aren't enough, your doctor can prescribe other treatments to reduce the pain. These include different types of drugs (some anticonvulsants and some antidepressants) that act as painkillers. Patches (called *Qutenza*) and cream containing capsaicin, a substance made from chilli peppers, may provide some pain relief.

A supplement called L-acetyl carnitine may help. Some people report that acupuncture has provided relief, although this is unproven

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scientifically. There is evidence that cannabis (marijuana) can help, as it is thought to have pain-killing properties. Bear in mind that cannabis use is illegal, that a safe dose for short-term or long-term use isn't known, and that there can be other health implications. Soaking feet in cold water, avoiding tight shoes and socks, avoiding long periods of standing and walking, and massage may provide relief.

If you have reduced sensation in your feet, there are some practical precautions you can take. Test the temperature of a bath with your elbow rather than your feet, check the soles of your feet regularly for damage, be careful when first wearing new shoes and avoid walking barefoot.

As there are several possible causes of nerve damage, it is very important to tell your doctor if you have tingling, numbness or pain in your feet so that the cause can be properly investigated.

Bone problems

Loss of bone density is more common in people with HIV than in the general population. There is a link between HIV itself and bone loss, possibly caused by HIV-related inflammation.

There is also a link between the anti-HIV drug tenofovir (*Viread*, also in the combination pills *Truvada*, *Atripla* and *Eviplera*) and bone problems. Some research has suggested there is also a possible link between bone loss and protease inhibitors.

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Overall, the benefits of being on HIV treatment outweighs an increased risk of bone loss. In many cases, people had other risk factors for bone problems. These include being older (and for women, having gone through the menopause), smoking, heavy drinking, being underweight, lack of exercise, a family history of bone loss, and low testosterone levels.

Your regular HIV monitoring will include blood tests to check the health of your bones. You may have additional tests as you get older, especially if you have other risk factors for bone loss. You can find out more in NAM's booklet *CD4, viral load & other tests*.

There are actions you can take to reduce the risk of bone loss, and to help slow it down

or deal with it if it does occur. These include eating a healthy diet, with enough calcium and vitamin D, getting some sunlight on your skin (for vitamin D production) and doing weight-bearing exercise. You can find out more about all of these in NAM's booklet *Nutrition*.

Summary

- HIV treatment is very effective and can mean a long and healthy life.
- However, anti-HIV drugs – like all medications – can cause unwanted side-effects.
- HIV treatment is meant to keep you well. You don't have to put up with side-effects.
- It's not inevitable that you will experience side-effects. If side-effects do develop, they will often go away. Otherwise, it's usually possible to do something about them.
- Some anti-HIV drugs can cause a serious hypersensitivity (allergic) reaction. You will be told about the symptoms to look out for and what to do if you experience them. It's important you take action quickly, and that you don't take the drug that caused that reaction again in the future.
- It always makes good sense to tell your doctor about any side-effects or symptoms you are experiencing.
- The side-effects caused by the most commonly used HIV drugs nowadays tend to be mild. You're most likely to notice side-effects soon after you start taking a new drug and these usually lessen or go away with time.

- Common side-effects are diarrhoea, feeling or being sick, headache, rash and tiredness. It's usually possible to take medicines to control these.
- Some side-effects develop after you've been taking a medicine for a period of months or even years. You'll have tests to check for these and it makes good sense to tell your doctor about any unusual symptoms.
- Some of the long-term side-effects that people are most anxious about, such as fat loss and fat gain (lipodystrophy), are mostly linked to drugs no longer used routinely in the UK.

Glossary

Allergic reaction Also called a hypersensitivity reaction, a reaction by the immune system to a substance, such as a medicine, that in most people would cause no symptoms.

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

Entry inhibitors Family of antiretrovirals that includes maraviroc.

Fusion inhibitors Family of antiretrovirals that includes T-20.

Glossary

Hypersensitivity Another word for allergy.

Clinical trial A research study, usually to find out how well a new drug or treatment works in people and how safe it is.

Integrase inhibitors The family of antiretrovirals that includes raltegravir.

NNRTI Non-nucleoside reverse transcriptase inhibitor, the family of antiretrovirals that includes efavirenz, etravirine, nevirapine and rilpivirine.

NRTI Nucleoside reverse transcriptase inhibitor, the family of antiretrovirals that includes 3TC, abacavir, AZT, d4T, ddI, FTC and tenofovir.

Protease inhibitor The family of antiretrovirals that includes atazanavir, darunavir, fosamprenavir, lopinavir/ritonavir, ritonavir and tipranavir.

Side-effect An unwanted secondary effect of a treatment. Also sometimes called an adverse event.

Resistance A drug-resistant HIV strain is one that is less sensitive to the effects of one or more anti-HIV drugs because of changes in its structure.

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Has this booklet helped you make decisions about your health and treatment?

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Yes

A little bit

No

Has this booklet made you feel more informed about key issues?

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Yes

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No

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Yes, very much

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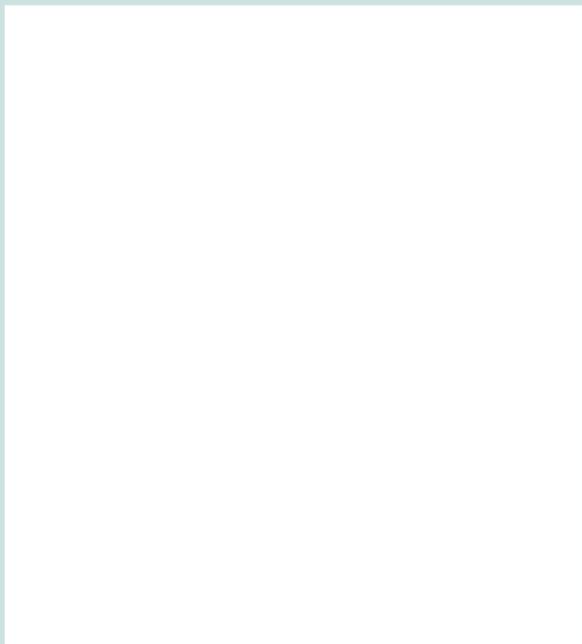
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From the Terrence Higgins Trust

Telephone 0808 802 1221

Opening hours Monday-Friday, 10am-8pm

HIV i-Base Treatment Phonenumber

Telephone 0808 800 6013

Opening hours Monday-Wednesday, 12pm-4pm

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Telephone 020 7713 0444

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NAM information series for HIV-positive people - visit www.aidsmap.com/booklets

The booklet series includes: ● Adherence & resistance ● Anti-HIV drugs ● CD4, viral load & other tests ● HIV & children ● HIV, GPs & other primary care ● HIV & hepatitis ● HIV, mental health & emotional wellbeing ● HIV & sex ● HIV, stigma & discrimination ● HIV & TB ● HIV & women ● Nutrition

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aidsmap.com

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