nam

information series for hiv-positive people

anti-hiv drugs

acknowledgments

This edition edited by Michael Carter

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NAM is a charity that publishes information for people affected by HIV and those working with them. We believe information helps people to make decisions about, and be in control of, their lives, health and treatment options.

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information series for hiv-positive people

anti-hiv drugs

This booklet is a starting point for anyone who wants to know about treatment for HIV and AIDS. It provides basic information about the drugs that fight HIV – known as antiretroviral drugs – and deals briefly with dosing, side-effects, drug interactions and drug resistance.

Information contained in this booklet has been reviewed by a panel of medical experts. For full details of side-effects and drug interactions, see the Product Information Leaflets which are produced by the drug manufacturers.

This information was correct at the time of going to press (June 2005). The booklet includes information on drugs which have been licensed in the UK or European Union.

This booklet has been written to help you decide what questions to ask your doctor about any course of treatment you might be considering. We don't intend for it to replace discussion with your doctor about your treatment.

contents

contents

HIV and anti-HIV drugs

HIV is a virus which attacks the immune system – the body's defence system against infection and illness. If you have HIV, you can take drugs to reduce the level of HIV in your body. By reducing the amount of HIV in your body, you can slow or prevent damage to your immune system. These drugs are not a cure, but they can help you stay well and extend your life. Anti-HIV drugs are known as antiretroviral drugs.

How antiretroviral drugs work

HIV mainly infects cells in the immune system called CD4 cells. Over many years of HIV infection, the number of CD4 cells drops gradually but continually and the immune system is weakened. If nothing is done to slow or halt this destruction of the immune system, a condition called AIDS (Acquired Immune Deficiency Syndrome) follows as your immune system is no longer able to fight infections. Antiretroviral drugs work by interrupting this process.

The aim of treatment

An untreated person with HIV may have thousands or even millions of HIV particles in every millilitre of blood. The aim of treatment is to reduce the amount of HIV to very low levels - below 50 copies per millilitre of blood.

To provide you with the best chance of reducing the amount of HIV in your blood to very low levels, your doctor may recommend that you take a powerful combination of at least three antiretroviral drugs. Once your viral load – the amount of HIV in your blood – has dropped, your immune system should begin to recover and your ability to fight infections is likely to improve.

When to take treatment

There are many opinions about the best time to start taking antiretroviral therapy but there is no general rule that applies to everyone. Some people take treatment early on, before there is much damage to the immune system; others start later, when blood tests show they are likely to become sick in the near future. Some people wait until they are sick before taking antiretrovirals.

Your decision about when to start therapy should be made in consultation with your doctor. If you are getting persistent 'minor' infections, or if you have had an AIDS-defining illness, (eg PCP), your immune system may already be seriously weakened. In this situation, your doctor will strongly advise you to consider taking antiretrovirals.

If you have established HIV infection but have no symptoms, current guidelines

recommend beginning therapy before your CD4 cell count falls below 200.

If your CD4 cell count is between 200 and 350 it is recommended that you consider starting therapy. In such circumstances you should use your recent viral load measurements and the number of CD4 cells you have been losing to guide your decision.

The final decision about when to begin treatment rests with you. Social factors such as family, plans to start a family, relationships, work and travel may influence your decision.

For more information see the booklet *HIV Therapy* in this series.

Sticking to your drug routine

Taking antiretroviral therapy is a long-term commitment. Once you start the drugs, it is recommended that you continue treatment for the rest of your life.

It is very important not to miss doses and to take the drugs as prescribed. If you miss doses, or you do not take the drugs as you are supposed to, the HIV in your body is more likely to develop resistance to the drugs. This will reduce their long-term effectiveness.

If you are having difficulty sticking to your drug routine, discuss alternative combinations that may be easier for you to take with your doctor.

There are many tips and aids which may improve your ability to take your drugs as required. For more information, speak to your health care team, or visit NAM's website *aidsmap.com*.

For more information see the booklets *Adherence* and *Resistance* which are produced by NAM.

Regular check-ups

If you have HIV, you should see a doctor regularly for a check-up. Most people with HIV attend GUM clinics or specialist HIV clinics which have doctors and other health professionals trained in HIV and AIDS. Even if you do not want to take treatments at this stage, regular blood tests will tell you how the disease is progressing.

If you are entitled to free NHS care, antiretroviral drugs provided through NHS HIV clinics and GUM clinics are free.

Monitoring

Before you start on antiretrovirals, or before you switch to a new combination, you should have a number of blood tests. Viral load and CD4 tests will tell you how advanced your HIV disease is. Once you have begun treatment, tests to measure liver function and fat and sugar levels in the blood may be conducted to assess the effects of the drugs on the normal

workings of your body. Your doctor may also test to see if the HIV has developed resistance to any of the antiretrovirals.

Once you are on a new combination, a viral load and CD4 cell count will be done within the first month of treatment. This is to check that the drugs are working. Testing is generally performed every three months, although some doctors may perform tests more regularly and some less often once you are well established on treatment and doing well.

For more information, see the booklet *Viral Load & CD4* produced by NAM in this series.

Pregnancy

Combinations of antiretrovirals are now commonly used during pregnancy as an effective means of preventing the transmission of HIV from a mother to her baby. However, the long-term effects on the child are not yet clear. Generally, anti-HIV drugs are not recommended during the first three months of pregnancy unless the woman is already on treatment.

As a woman's health improves on antiretrovirals, her fertility may also increase. It is recommended that women considering pregnancy, or women who may conceive, discuss their treatment options with their doctor before conceiving.

You should tell your HIV doctor or another member of your health care team immediately if you become pregnant. The contraceptive pill is less effective in women on anti-HIV drugs due to drug interactions.

There is no evidence that a father's treatment increases the risk of birth defects.

For more information, see the booklets *HIV and children* and *HIV and women* produced by NAM in this series.

Side-effects

It is very common for people to experience side-effects to antiretroviral therapy, especially during the first few weeks of treatment. Your doctor can prescribe a number of drugs to help you cope with this initial period.

Common side-effects of many medications include headache, nausea, diarrhoea, and tiredness. Report side-effects, especially rash and fever, to your doctor promptly.

In this booklet, we have listed as common side-effects anything which affected more than 5-10% of people in clinical trials of a drug, and which are therefore likely to be side-effects of the drug.

Drug interactions

Taking two or more different drugs together may result in an alteration in the effectiveness (or toxicity) of one or more of the drugs being taken. This booklet lists the key drug interactions for antiretroviral drugs.

Some antiretroviral drugs lower or increase levels of other antiretroviral drugs. Some antiretroviral drugs interact with other medicines commonly used in the treatment of HIV.

Some drug combinations are contraindicated – which means you definitely should not take them together. Reasons for this include serious toxicity and interactions which make one or both drugs ineffective.

Other interactions are less serious. Levels of one or both drugs in your blood may be affected and dosing adjustments may be required.

Some drug interactions may mean that you have a greater chance of developing certain side-effects such as peripheral neuropathy.

Less is known about interactions with recreational drugs. However, if you use recreational drugs, it is sensible to discuss this with your doctor, HIV pharmacist or other health care provider.

Protease inhibitors are the class of antiretrovirals most likely to interact with recreational drugs, though interactions with both NRTIs and NNRTIs and recreational drugs have been described.

Antiretrovirals can also interact with herbal and alternative treatments. It is known that the herbal antidepressant St John's wort lowers blood levels of both NNRTIs and protease inhibitors. Garlic capsules stop the protease inhibitor saquinavir from working properly and it is thought that they could have a similar effect on other protease inhibitors as well. Test tube studies have recently indicated that African potato and *Sutherlandia*, two herbs widely used to treat HIV in Africa, interfere with the body's ability to process protease inhibitors and NNRTIs.

Interactions can even happen with medicines that are not taken by mouth. For example, ritonavir can interact with inhalers and nasal sprays containing fluticasone (eg *Flixotide*™ and *Flixonase*™) causing serious side-effects.

To help increase the chances of all your drugs working effectively and to minimise the possibility of side-effects, make sure you tell your clinic doctor and HIV pharmacist about **all** the medicines that you are taking. Also check before taking anything new (whether you buy it yourself or have it prescribed by a doctor or dentist).

What's in a name?

Pharmaceutical drugs are given several names:

- First, a research name based on its chemical make-up or manufacturer, eg DMP266.
- Second, a generic name which is common to all pharmaceuticals with that chemical make-up, eg efavirenz.
- Third, a brand name which belongs to a particular company. A brand name starts with a capital letter and is generally written in italics, eg *Sustiva*™.

This booklet lists all three names at the start of a drug entry. The most common name for each drug is used in the text.

10 Types of antiretroviral drugs

There are five main types of antiretroviral drugs:

- **nucleoside analogue reverse transcriptase inhibitors** (NRTIs), which target an HIV protein called reverse transcriptase.
- **non-nucleoside reverse transcriptase inhibitors** (NNRTIs), which also target reverse transcriptase.
- **nucleotide analogue reverse transcriptase inhibitors** (NtRTIs), which also target reverse transcriptase.
- **protease inhibitors** (PIs), which target an HIV protein called protease.
- **fusion inhibitors**, which target the point where HIV binds onto cells of the immune system.

Each class of drug attacks HIV in a different way. Generally drugs from two (or sometimes three) classes are combined to ensure a powerful attack on HIV.

Where antiretrovirals block HIV

fusion
Fusion inhibitors work here by targeting the point where HIV locks onto an immune cell.

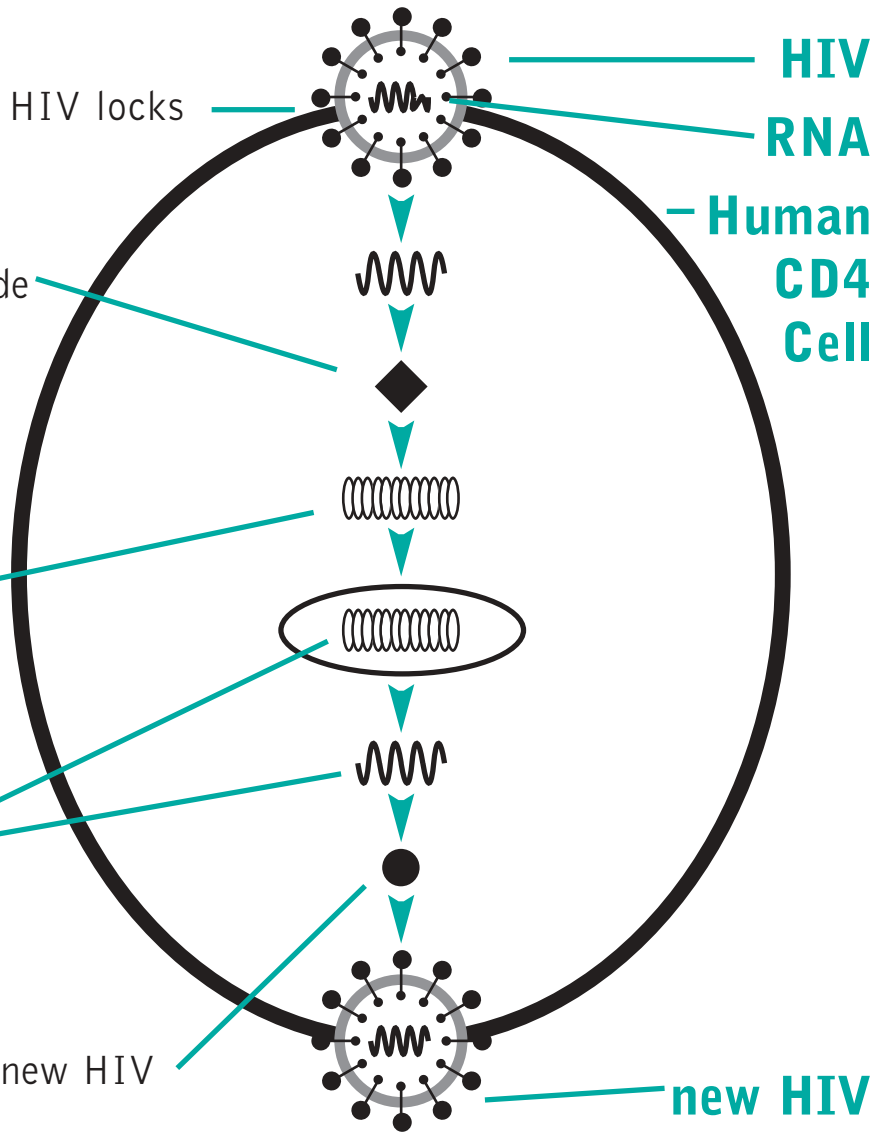
reverse transcription (reverse transcriptase)
Non-nucleoside reverse transcriptase inhibitors, nucleoside analogue reverse transcriptase inhibitors and nucleotide analogue reverse transcriptase inhibitors work here. When HIV has entered the cell, it uses reverse transcriptase to convert itself into viral DNA.

viral DNA
When HIV has entered the cell it uses reverse transcriptase to convert itself into viral DNA.

integration
Viral DNA is inserted into human DNA in the nucleus.

transcription and translation
New viral material.

viral assembly
Protease inhibitors work here. Protease is used to make new HIV from viral material made in the nucleus.



Nucleoside analogue reverse transcriptase inhibitors (NRTIs)

NRTIs are normally the basis or 'backbone' of any anti-HIV drug combination. NRTIs may also be called nukes. The NRTIs are:

- 3TC, lamivudine, *Epivir*™
- abacavir, *Ziagen*™
- AZT, zidovudine, *Retrovir*™
- *Combivir*™, (3TC and AZT)
- *Kivexa*™, (abacavir and 3TC)
- *Trizivir*™, (3TC, AZT and abacavir)
- d4T, stavudine, *Zerit*™, *Zerit PRC*™
- ddC, zalcitabine, *Hivid*™
- ddI, didanosine, *Videx*™, *Videx EC*™
- FTC, emtricitabine, *Emtriva*™

Common dual combinations of NRTIs that are used as a part of three or four drug combinations are:

- AZT/3TC (often given as a combined pill called *Combivir*™)
- 3TC/abacavir (often given in a combined pill called *Kivexa*™)
- d4T/3TC, AZT/ddI

Combinations that should be avoided are:

- d4T/AZT, d4T/ddC, d4T/ddI, 3TC/ddC and ddI/ddC

The combination of ddI with the nucleotide analogue tenofovir should only be taken in exceptional circumstances and avoided whenever possible.

The nucleoside analogue FTC (emtricitabine) is often used with the nucleotide analogue tenofovir (often given in a combined pill called *Truvada*™).

Trizivir™ is a combination tablet containing three nucleoside analogues (AZT, 3TC, abacavir).

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

An NNRTI is often taken with two NRTIs as an alternative to a protease inhibitor. NNRTIs may also be called 'non-nukes'.

Two NNRTIs are currently approved for use in the UK:

- efavirenz, *Sustiva*™
- nevirapine, *Viramune*™

Nucleotide analogue reverse transcriptase inhibitors (NtRTIs)

Nucleotide analogues also work against reverse transcriptase, and are usually used in place of an NRTI in a three drug combination. One nucleotide analogue is approved in the UK:

- tenofovir, *Viread*™

Tenofovir is also available in a combination tablet with the nucleoside analogue FTC (emtricitabine, *Emtriva*™) called *Truvada*™.

Protease inhibitors (PIs)

Protease inhibitors were the second class of antiretroviral drugs to be available on prescription. The protease inhibitors in current use are:

- amprenavir, *Agenerase*™
- fosamprenavir, *Telzir*™
- atazanavir, *Reyataz*™
- indinavir, *Crixivan*™
- lopinavir/ritonavir, *Kaletra*™
- nelfinavir, *Viracept*™
- ritonavir, *Norvir*™
- saquinavir hard gel and tablet, *Invirase*™
- saquinavir soft gel, *Fortovase*™

People who choose to take a combination containing a protease inhibitor often take a protease inhibitor 'boosted' by a small dose of ritonavir, as well as taking two NRTIs. Common 'boosted' protease inhibitors are: ritonavir/saquinavir, indinavir/ritonavir, lopinavir/ritonavir, amprenavir/ritonavir, atazanavir/ritonavir.

Other combinations may include one or two protease inhibitors, one NNRTI, and one or two NRTIs. If a person's initial combination has not worked, some doctors may recommend a combination of four or more antiretrovirals.

Fusion inhibitors

Fusion inhibitors stop HIV from binding to and entering the human cell. One fusion inhibitor, T20 (enfuvirtide, *Fuzeon*™), has been approved and is given by a subcutaneous injection (similar to the way diabetes inject insulin). It is only available to people who have been extensively pre-treated with other anti-HIV drugs and have very limited treatment options available to them.

- T-20, enfuvirtide, *Fuzeon*™

16 Nucleoside analogue reverse transcriptase inhibitors (NRTIs)

3TC

Names: 3TC, lamivudine, *Epivir*™

Approved dosage: 300mg daily, either as one white 150mg tablet twice a day or two white 150mg tablets once a day or once white 300mg tablet once a day. The dose may be altered if you have impaired kidney function. Also available in a combined form with AZT called *Combivir*™ and in a combined form with AZT and abacavir called *Trizivir*™. 3TC and abacavir are also available in a combined formulation called *Kivexa*™. *Combivir*™ and *Trizivir*™ are both taken as one tablet twice a day and *Kivexa*™ is taken as one tablet once a day.

Children: approved for use in children. Liquid suspension available.

Tips on taking it: take with or without food.

Common side-effects: headache, tiredness.

Rare side-effects: rash, diarrhoea, nausea, abdominal pain, blood disorders, peripheral neuropathy, insomnia and liver problems.

Resistance to 3TC: may affect your response to abacavir. Drug-resistant 3TC may continue to have an antiviral effect. People who have virus resistant to 3TC are unlikely to respond to FTC.

Key drug interactions: few significant drug interactions. Any drug that causes

neutropenia may increase side-effects. 3TC should not be taken with intravenous foscarnet or ganciclovir.

abacavir

Names: abacavir, *Ziagen*™

Approved dosage: 600mg daily, either as one 300mg yellow tablet twice daily or two 300mg tablets once a day. Also available in a combined form with AZT and 3TC (*Trizivir*™, taken as one tablet twice daily). Abacavir and 3TC are also available in a combined formulation called *Kivexa*™. The combined *Kivexa*™ pill contains 600mg of abacavir and 300mg of 3TC and the dose is one tablet taken once daily.

Children: liquid formulation available.

Tips on taking it: take with or without food.

Common side-effects: nausea and vomiting, headaches, weakness, diarrhoea, insomnia, dizziness, and abdominal pain.

Rare side-effects: An allergic reaction (often involving fever and rash) occurs in 3-6% of people taking abacavir, usually within four weeks of starting the drug. See your doctor immediately if you develop a rash, fever or abdominal pain while on abacavir. You should not re-try abacavir, or take *Trizivir*™ or *Kivexa*™if you have had an allergic reaction to abacavir previously. Liver problems can also be a rare side-effect of the drug.

Resistance to abacavir: may affect your response to AZT, 3TC, ddI and possibly tenofovir.

Key drug interactions: no significant drug interactions yet identified.

Brain: abacavir may cross the blood-brain barrier and may be effective against HIV in the brain.

Kivexa™

Abacavir and 3TC are available in a combined form called *Kivexa*™. The dosage of *Kivexa*™ is one orange tablet (600mg abacavir and 300mg 3TC) once a day. See the entries for abacavir and 3TC for side-effects.

AZT

Names: AZT, zidovudine, *Retrovir*™

Approved dosage: one white and blue 250mg capsule taken twice a day. A 100mg capsule is available for dose variations.

Children: approved for use in children. Liquid formulation available.

Tips on taking it: try to take the doses twelve hours apart. Take with or after food to reduce nausea. Anti-nausea drugs may be used up-front.

Common side-effects: nausea, vomiting, fatigue, headache, insomnia, blood disorders.

Rare side-effect: liver problems.

Resistance to AZT: is likely to cause resistance to d4T and possibly also to abacavir and tenofovir.

Key drug interactions: other drugs (eg hydroxyurea, ganciclovir) that cause blood disorders may worsen side-effects. Do not take with d4T. Drug levels may be affected if methadone, phenytoin, or probenecid are taken with AZT. Doses of clarithromycin and AZT should be taken one hour apart.

Brain: AZT is effective against HIV in the brain and the central nervous system.

Combivir™

AZT is also available in a combined form with 3TC called *Combivir*™. Dosage of *Combivir*™ is one white tablet (150mg 3TC and 300mg AZT) twice a day. See the entry for AZT and 3TC for side-effects.

Trizivir™

AZT is also available in a combined form with 3TC and abacavir called *Trizivir*™. Dosage of *Trizivir*™ is one green tablet (300mg AZT, 150mg 3TC and 300mg abacavir) taken twice a day. See the entries for AZT, 3TC and abacavir for side-effects.

d4T

Names: d4T, stavudine, *Zerit*™, *Zerit PRC*™

Approved dosage: for people over 60kg (91/2 stone): one dark orange 40mg capsule twice a day; for people under 60kg: usually one light and dark orange 30mg capsule twice a day.

Note: people with impaired kidney function or peripheral neuropathy may take 15 or 20mg twice a day. d4T is available as 40mg, 30mg, 20mg and 15mg capsules.

Zerit PRC™ is approved for once daily dosing. The dose for people weighing over 60kg is 100mg, and for people weighing less than 60kg, 75mg a day.

Children: approved for use in children. d4T comes in a powder form.

Tips on taking it: although the product information advises taking d4T on an empty stomach, this does not affect absorption of the drug and it is possible to take with or without food. However, taking it with food reduces nausea.

Common side-effects: peripheral neuropathy, headache, nausea, diarrhoea or constipation.

Rare side-effects: pancreatitis, liver problems.

Resistance to d4T: likely to cause resistance to AZT.

Key drug interactions: do not take with AZT. Drugs that may cause peripheral neuropathy or pancreatitis (eg ddI) may increase the risk of these side-effects.

Brain: d4T crosses the blood-brain barrier and may be effective against HIV in the brain.

ddC

Names: ddC, zalcitabine, *Hivid*™

Approved dosage: one pale blue/grey 0.75mg tablet three times a day.

Children: syrup available for children through a special access scheme.

Tips on taking it: take with or after food to reduce nausea.

Common side-effects: peripheral neuropathy, mouth ulcers, diarrhoea, nausea, rash.

Rare side-effects: pancreatitis (very rare), liver problems.

Resistance to ddC: low risk of resistance to ddI, 3TC and abacavir.

Key drug interactions: do not take with ddI or 3TC. Other drugs that can cause peripheral neuropathy, pancreatitis, or ulcers increase the risk of these side-effects of ddC.

Note: Roche Pharmaceuticals, who make ddC, have announced that they plan to stop making it in 2006 or shortly after.

ddI (*Videx*™)

ddI is available in two formulations, as a tablet and capsule. Advice on taking ddI differs depending upon which formulation you are taking.

Names: ddI, didanosine, *Videx*™

Approved dosage: for people over 60kg (91/2 stone): two white, orange-flavoured 200mg tablets once daily; for people under 60kg: one large white, orange-flavoured 200mg tablet plus two large white, orange flavoured 25mg tablets one a day. Note: people who have kidney or liver abnormalities may be advised by their doctor to take a lower dose.

Children: approved for use in children. Liquid formulation available.

Tips on taking it: take on an empty stomach to maximise the amount of ddI that gets into your blood. Take ddI tablets at least two hours after eating and wait another half an hour before eating again. During this fasting period avoid fruit juices (except clear apple juice), fizzy drinks and milk. Smoking may also reduce the absorption of ddI. Crush and dissolve ddI tablets in ice-cold water or clear apple

juice. If you take a dose first thing in the morning, dissolve your dose the night before and leave in the fridge. Pill-crushers are available from pharmacies.

Common side-effects: diarrhoea, peripheral neuropathy, nausea.

Rare side-effects: pancreatitis, greater risk if you have high alcohol consumption and/or liver problems.

Resistance to ddI: low risk of resistance to ddC, 3TC and abacavir.

Key drug interactions: ddI tablets should be taken at least two hours apart from any medicines which carry the warning 'not to be taken at the same time of day as indigestion remedies', as the effectiveness of these other medicines may be reduced. Examples of drugs which should not be taken at the same time as ddI tablets are atazanavir, itraconazole, ketoconazole, indinavir, ciprofloxacin, valganciclovir, tetracycline antibiotics and delavirdine (an NNRTI, not licensed in the UK). Do not take with ddC, allopurinol or intravenous pentamidine. Drugs such as H2 blockers, omeprazole, rifampicin, and rifabutin may increase the risk of pancreatitis. ddI tablets should not be taken at the same time of day as some other medications. For example, ddI

tablets and protease inhibitors must be taken at least one hour apart. Tenofovir increases ddI levels and they should only be taken in combination with ddI if no other options are available. If you do need to take ddI and tenfovir, you should be very closely monitored by your clinic and ddI should be taken at least two hours after or one hour before tenofovir.

When taken with hydroxyurea, the amount of active ddI in cells increases. Hydroxyurea may therefore both improve the effectiveness of ddI and increase the risk of side-effects, but is not licensed for use in this way.

ddI (*Videx EC*™)

Names: ddI EC capsules, didanosine enteric coated, *Videx EC*™

Approved dosage: for people over 60kg (9 1/2 stone): one 400mg white capsule once a day, or one 200mg capsule twice a day; for people under 60kg: one 250mg capsule once a day or one 125mg capsule twice daily.

Note: people who have kidney or liver abnormalities may be advised by their doctor to take a lower dose.

Children: ddI EC is approved for use in children.

Tips on taking it: take with water on an empty stomach to maximise the amount of ddI EC that gets into your blood. Take ddI EC capsules at least two hours before and two hours after food. Taking the capsules before bedtime may be most convenient. During this fasting period avoid all liquids except water. It is okay to take ddI EC at the same time as other antiretrovirals, including indinavir, so long as they do not need to be taken with food. ddI EC does not interact with medicines that should not be taken at the same time as indigestion remedies.

Common side-effects: diarrhoea, nausea, headache, peripheral neuropathy.

Rare side-effects: pancreatitis, liver problems.

Resistance to ddI: low risk of resistance to ddC, 3TC and abacavir.

FTC (emtricitabine, *Emtriva*™)

Names: FTC, emtricitabine, *Emtriva*™

Approved dosage: one blue and white 200mg capsule once a day.

Note: people who have kidney adnormalities may be advised by their doctor to take a lower dose.

Children: approved for use by children aged four months and over.

Tips on taking it: can be taken with or without food.

Common side-effects: dizziness, headache, diarrhoea, and nausea.

Less common side-effects: rash, vomiting, sleep problems, abnormal kidney and liver function, lactic acidosis, skin discolouration.

Resistance to FTC: unlikely to be beneficial for people who are already resistant to 3TC or abacavir.

Truvada™

FTC (emtricitabine) is also available in a combined pill with the nucleotide analogue, tenofovir. The FTC/tenofovir pill is called *Truvada*™. The dose is one blue tablet (200mg FTC and 300mg tenofovir) once a day. For side-effects see the entries for FTC and tenofovir.

efavirenz

Names: efavirenz, *Sustiva*™

Approved dosage: one orange 600mg tablet once a day or three orange 200mg capsules once a day.

Children: approved for use in children aged three years and above, who weigh more than 13kg. Oral solution available.

Tips on taking it: take with or without food. Avoid taking it with a high fat meal which may increase absorption. If efavirenz causes confusion or dizziness, take before going to bed.

Common side-effects: dizziness, diarrhoea, headache, rash. Psychological effects, most common during the first four weeks of treatment, include feeling 'out of sorts', confusion, vivid dreams, euphoria, suicidal thoughts, psychotic episodes.

Rare side-effects: Stevens-Johnson Syndrome (very rare), alcohol intolerance, fever, asthma, aches and pains, fatigue, dry mouth, raised total cholesterol, pancreatitis, blurred vision.

Resistance to efavirenz: is likely to cause resistance to delavirdine (an NNRTI that is not licensed for use in the UK) and nevirapine.

Key drug interactions: alters blood levels of protease inhibitors. May interfere with oral contraceptives. Do not take efavirenz

with hard gel saquinavir, St John's wort, clarithromycin, terfenadine, astemizole, cisapride, triazolam, rifampicin and midazolam. Drug levels may be affected if taken with *Viagra*™, *Cialis*™, *Levitra*™, *Zyban*™ or rifabutin.

Brain: efavirenz crosses the blood-brain barrier and has some action against HIV in the brain and the central nervous system.

Pregnancy: efavirenz is not recommended during pregnancy or in people planning pregnancy.

nevirapine

Names: nevirapine, *Viramune*™

Approved dosage: one white 200mg tablet once a day for the first two weeks and then one 200mg tablet twice a day thereafter. Men should not start treatment with nevirapine if their CD4 cell count is above 400, women should not start treatment with nevirapine if their CD4 cell count is above 250 as this increases the risk of potentially dangerous side-effects.

Experimental dosage: two white 200mg tablets once a day. This is not normally recommended within the first two months of taking nevirapine.

Children: syrup available.

Tips on taking it: take with or without food.

Common side-effects: rash, fatigue, liver problems, muscle pain, depression.

Rare side-effect: Stevens-Johnson Syndrome.

Resistance to nevirapine: is likely to cause resistance to delavirdine (an NNRTI that is not licensed in the UK) and efavirenz.

Key drug interactions: drug levels may be affected if nevirapine is taken with a number of drugs including atazanavir, indinavir, lopinavir/ritonavir, ketoconazole, *Cialis*™, *Viagra*™, *Levitra*™. Nevirapine may reduce the effectiveness of oral contraceptives. Drugs that may worsen side-effects are clarithromycin, erythromycin and amoxicillin. Do not take with St John's wort.

Brain: nevirapine may have some effect against HIV in the brain.

30 Nucleotide analogue reverse transcriptase inhibitors (NtRTIs)

tenofovir

Names: tenofovir, *Viread*™

Approved dosage: One blue, almond shaped film-coated 300mg tablet daily. Dose may be adjusted if kidney function impaired.

Tips on taking it: take with food, to increase absorption. If you are also taking ddI, take tenofovir two hours before or one hour after ddI.

Common side-effects: diarrhoea, nausea.

Rare side-effects: longer-term side-effects of tenofovir are not yet established, however there are some reports of kidney toxicities. Creatinine monitoring advised to spot kidney damage, especially in patients with impaired kidney function.

Resistance to tenofovir: may cause resistance to ddI and ddC.

Key drug interactions: tenofovir increases levels of ddI.

Truvada™

Tenofovir is also available in a combined pill with the nucleoside analogue, FTC (emtricitabine). The tenofovir/FTC pill is called *Truvada*™. The dose is one blue tablet (300mg tenofovir and 200mg FTC) once a day.

amprenavir

Names: amprenavir, *Agenerase*™, fosamprenavir, *Telzir*™

Approved dosage: eight cream 150mg capsules twice a day. Dose reductions may be recommended due to liver impairment or drug interactions. Approved for use in people over four years of age who have failed previous protease inhibitor-containing therapy. Note: production of amprenavir 150mg capsules ceased in late 2004 and hospitals in the UK are currently using their remaining stock.

A new version of amprenavir called fosamprenavir (*Telzir*™) has been developed. Its chief advantage is that it requires fewer capsules each day, and there will be more of the drug available in the blood to suppress HIV. This version of amprenavir can also be boosted with the other protease inhibitor ritonavir (*Norvir*™). The dose of the drug is one mauve 700mg tablet with one cream 100mg capsule of ritonavir twice daily.

Children: liquid formulation available for children over four years.

Tips on taking it: take with or without food. Liquid formulation not recommended for children under four years, pregnant women or individuals with liver damage, due to severe side-effects. Use with

caution in people with kidney impairment.

Common side-effects: headache, nausea, vomiting, diarrhoea, rash, fatigue, tingling around the mouth, lipodystrophy and metabolic abnormalities. Oral solution may also cause seizure, stupor, fast heart beat, blood disorders.

Resistance to amprenavir: likely to cause resistance to ritonavir, and possibly also to saquinavir, indinavir and nelfinavir.

Key drug interactions: don't take with rifampicin, terfenadine, astemizole, cisapride, triazolam, midazolam, ergot medications, bepridil and St John's wort. Dose adjustments may be required when amprenavir is taken with erythromycin, rifabutin, efavirenz, indinavir, ritonavir, nelfinavir, amiodarone, phenobarbitonel, phenytoin, lidocain, warfarin, quinidine, nortriptyline, imipramine, *Viagra*™, *Cialis*™, *Zyban*™, *Levitra*™, amitryptyline and desipramine. Amprenavir contains high levels of vitamin E, so supplements containing vitamin E should not be taken at the same time as amprenavir. However, you can take supplements containing vitamin E if you are taking fosamprenavir.

atazanavir

Names: atazanavir, *Reyataz*™

Approved dosage: 300mg (two light and dark blue 150mg capsules) plus one cream

100mg ritonavir capsule taken together once a day. If the combination also contains efavirenz or nevirapine the dose is 400mg (two turquoise 200mg capsules) plus one 100mg ritonavir capsule taken together once a day.

Tips on taking it: take with food.

Common side-effects: diarrhoea.

Rare side-effects: abnormal liver function, jaundice.

Resistance to atazanavir: there is conflicting evidence. Early studies suggested that atazanavir would be effective in people resistant to other protease inhibitors. However, more recent evidence shows that as many as 40% of people who had previously used a protease inhibitor would have reduced sensitivity to the drug. This is why it is recommended to boost atazanavir levels with ritonavir.

Key drug interactions: when taken with efavirenz or tenofovir, levels of atazanavir drop. However, adding 100mg of ritonavir counters this. Take ddI tablets at least two hours before or one hour after atazanavir (not necessary if taking *Videx EC*™). Doses of the anti-TB drug rifabutin should be reduced by 75%. Reduce doses of clarithromycin by half if taken at the same time as atazanavir. Reduce doses of

Cialis™, *Viagra*™, or *Levitra*™ by half. Don't take with St John's wort. Don't take antacids within four hours of atazanavir. Don't t take lansoprazole, omeprazole, rifampicin, phenytoin, carbamazepine, or simvastatin with atazanavir.

indinavir

Names: indinavir, *Crixivan*™

Approved dosage: 800mg (two cream 400mg capsules) every eight hours.

Experimental dosage: with ritonavir: 400mg of both drugs twice daily. Alternatively, two 400mg capsules of indinavir and 100mg of ritonavir twice a day, or two 400mg capsules of indinavir and 200mg of ritonavir (other doses have been used in conjunction with drug level monitoring studies).

Tips on taking it: when indinavir is taken without ritonavir it should ideally be taken on an empty stomach (avoiding food for two hours before and one hour after each dose). Alternatively it can be taken with a light, low-fat snack, eg 30g cereal with 100g skimmed milk or a tea or coffee with sugar and skimmed milk plus one biscuit, or two small slices of toast with low-fat spread and 15g of jam per slice. For more suggestions, see NAM's *Nutrition* booklet, or discuss your options with an HIV dietitian. If indinavir is taken with

ritonavir, there are no food restrictions. Drink 1.5 litres of water or a non-caffeinated drink in addition to your usual fluid intake, to reduce the risk of kidney stones. Indinavir must be stored with a desiccant to keep the capsules dry. Can be kept in a dosette box without a desiccant for up to three days.

Common side-effects: kidney stones, pain when urinating, tiny stones in urine, dry lips and skin, liver abnormalities, nausea, lipodystrophy and metabolic abnormalities. Low fluid intake will increase your risk of developing kidney problems.

Rare side-effects: diabetes.

Resistance to indinavir: causes resistance to ritonavir, and is likely to cause resistance to saquinavir, nelfinavir and amprenavir.

Key drug interactions: do not take indinavir with St John's wort, terfenadine, astemizole, cisapride, alprazolam, pimozide, rifampicin, amiodarone, quinidine and ergot alkaloids. Careful monitoring and dose adjustments may be needed if indinavir is taken with drugs including: rifabutin, ketoconazole, the NNRTIs, *Viagra*™, *Cialis*™, *Levitra*™ and simvastatin. Large doses of vitamin C have been shown to reduce indinavir concentrations in the blood.

lopinavir/ritonavir (*Kaletra*™)

Names: lopinavir/ritonavir, ABT-378/r, *Kaletra*™

Approved dosage: 400mg lopinavir plus 100mg ritonavir (three orange 133.3mg/33.3mg capsules) twice daily. The dose is increased to four capsules when taken with efavirenz or nevirapine.

Children: approved for children over two years. Liquid formulation available.

Tips on taking it: take with food. *Kaletra*™ should be kept in the fridge. However it can be stored at room temperature (below 25 degrees C) for up to six weeks.

Common side-effects: diarrhoea and loose stools, headache, nausea, vomiting, stomach pain, fatigue, rash, metabolic abnormalities and raised liver enzymes. It is possible that lipodystrophy, a side-effect of other protease inhibitors, will also affect lopinavir/ritonavir users.

Resistance to lopinavir/ritonavir: likely cross-resistance with indinavir and ritonavir and, to some extent, amprenavir. High level resistance to other protease inhibitors may reduce the effectiveness of lopinavir/ritonavir, but lopinavir/ritonavir appears effective against virus resistant to other protease inhibitors.

Key drug interactions: due to the presence of ritonavir, avoid all drugs which negatively interact with ritonavir (see ritonavir entry). Efavirenz and nevirapine reduce levels of lopinavir/ritonavir and dose adjustments are recommended. Lopinavir/ritonavir reduces levels of amprenavir. Do not take with St John's wort. Monitoring and dose adjustment may be necessary when lopinavir/ritonavir is taken in conjunction with amiodarone, bepredil, quinidine, systemic lidocaine, warfarin, calcium channel blockers, *Viagra*™, *Cialis*™, *Levitra*™, Zyban™, tacrolimus, cyclosporin, methadone, rifabutin, rifampicin, oral contraceptives, ketoconazole and itraconazole.

nelfinavir

Names: nelfinavir, *Viracept*™

Approved dosage: five blue 250mg tablets twice a day, or three blue 250mg tablets three times a day.

Children: nelfinavir is approved for use in children. Available in powder form.

Tips on taking it: it is very important that you take nelfinavir with food to increase absorption.

Common side-effects: diarrhoea, nausea, lipodystrophy and metabolic abnormalities.

Resistance to nelfinavir: is likely to cause resistance to saquinavir and may cause resistance to ritonavir and indinavir.

Key drug interactions: careful monitoring and dose adjustments may be needed if nelfinavir is taken with drugs including: oral contraceptives, rifabutin, methadone, carbamazapine, phenytoin, *Viagra*™, *Cialis*™, *Zyban*™, *Levitra*™ and some lipid-lowering drugs. Do not take nelfinavir with terfenadine, rifampicin, astemizole, cisapride, pimozide, amiodarone, quinidine, midazole, triazolam, simvastin, ergot alkaloids or St John's wort.

ritonavir

Names: ritonavir, *Norvir*™

Approved dosage: six 100mg cream capsules twice a day. Alternatively, 7.5ml of ritonavir liquid twice daily. Start on a low dose and increase over 14 days to minimise side-effects.

Ritonavir is also used in small doses (usually 100mg or 200mg once or twice daily) to 'boost' other protease inhibitors. It has been approved for use in this way in the following doses: ritonavir/amprenavir 100/600mg twice daily; ritonavir/fosamprenavir 100/700mg twice daily; ritonavir/atazanavir 100/300mg once daily; ritonavir/saquinavir 100mg/1000mg twice daily.

Experimental dosage: ritonavir/saquinavir 400/400mg twice daily; ritonavir/indinavir 400/400mg or 200/800mg or 100/800mg twice daily.

Children: ritonavir is not formally approved for use in children, although it can be made available.

Tips on taking it: take with food to reduce nausea. If taking the liquid, try mixing it with a milk-based nutritional supplement. Do not mix with water, fizzy drinks or fruit juice. To disguise the taste, suck ice cubes or icy fruit juice before and after your dose. Alternatively, follow ritonavir with chocolate, mango, peanut butter, salty crisps or other food with strong flavour. *Norvir*™ capsules should be stored in a fridge, but can be kept at room temperature (below 25 degrees C) for up to 30 days. Ritonavir liquid should always be stored at room temperature.

Common side-effects: diarrhoea, stomach pain, nausea, vomiting, weakness, taste abnormalities, loss of appetite, numbness around the mouth, lipodystrophy and metabolic abnormalities.

Rare side-effects: kidney problems, diabetes.

Resistance to ritonavir: causes resistance to indinavir and is likely to mean some resistance to nelfinavir, saquinavir and amprenavir.

Key drug interactions: ritonavir interacts with many other medications. Consult your doctor or HIV pharmacist before taking any other drugs with ritonavir (including inhalers, medicines bought from a high street chemist, herbal preparations and

recreational drugs). Do not take ritonavir with piroxicam, dextropropoxyphene, pethidine; amiodarone, encainide, flecainide, propafenone, quinidine, bupropion (*Zyban*™, astemizole, terfenadine, clozapine, pimozide, alprazolam, clorazepate, diazepam, estazolam, bepridil, cisapride; fluorazepam, midazolam, triazolam, zolpidem, *Viagra*™, *Cialis*™ *Levitra*™ or St John's wort.

saquinavir (*Invirase*™)

Saquinavir is available in two formulations: as a hard gel capsule called *Invirase*™, or a soft gel capsule called *Fortovase*™. Advice on taking saquinavir differs depending upon which formulation you are taking.

Names: saquinavir (hard gel), *Invirase*™

Approved dosage: two orange 500mg tablets (or five yellow and green 200mg capsules) together with one 100mg capsule of ritonavir twice a day.

Children: *Invirase*™ is not approved for use by children.

Tips on taking it: take *Invirase*™ within two hours of a full meal to increase absorption.

Common side-effects: diarrhoea, stomach pain, nausea, lipodystrophy and metabolic disorders.

Rare side-effects: diabetes.

Resistance to saquinavir: may mean resistance to nelfinavir, indinavir and ritonavir.

Key drug interactions: do not take with rifampicin, rifabutin, astemizole, terfenadine, cisapride or the herbal anti-depressant St John's wort. Careful monitoring and dose adjustments may be needed if taking saquinavir with many other drugs including: NNRTIs, methadone, anti-arrhythmics, some anti-depressants, some anti-convulsants, some lipid-lowering drugs, dapsone, ergotamine, dihydroergotamine, dexamethasone, *Viagra*™, *Cialis*™ and *Levitra*™. Do not take with garlic supplements. If combined with ritonavir, drug interactions may change.

saquinavir (*Fortovase*™)

Names: saquinavir (soft gel), *Fortovase*™

Approved dosage: six cream 200mg capsules three times a day.

Experimental dosages: if taking *Fortovase*™ twice daily, take eight capsules twice a day. With 400mg ritonavir, take two 200mg capsules of *Fortovase*™ twice a day. With nelfinavir, take five nelfinavir 250mg tablets and six 200mg capsules of *Fortovase*™ twice a day.

Children: *Fortovase*™ is not available to children.

Tips on taking it: take *Fortovase*™ within two hours of food. *Fortovase*™ should be stored in a fridge. But it can be kept at room temperature (below 25 degrees C) for up to three months.

Common side-effects: diarrhoea, stomach pain, nausea, lipodystrophy and metabolic abnormalities.

Rare side-effects: diabetes.

Resistance to saquinavir: may mean resistance to nelfinavir, indinavir and ritonavir.

Key drug interactions: do not take with rifampicin, rifabutin, astemizole, terfenadine, cisapride or the herbal anti-depressant St John's wort. Careful monitoring and dose adjustments may be needed if taking saquinavir with many other drugs including: NNRTIs, methadone, anti-arrhythmics, some anti-depressants, some anti-convulsants, some lipid-lowering drugs, dapsone, ergotamine, dihydroergotamine, dexamethasone, *Viagra*™, *Cialis*™ and *Levitra*™. Do not take with garlic supplements. If combined with ritonavir, drug interactions may change.

Note: Roche Pharmaceuticals, the manufacturers of *Fortovase*™ have announced that they will cease its production in 2006 or soon after.

T-20

Names: T-20, enfuvirtide, *Fuzeon*™

Approved dosage: 90mg (one injection under the skin) twice a day. The drug has to be made up from powder.

Tips on taking it: extensive support and advice is available to people prescribed T-20. Doses can be prepared within 24 hours of use, so two doses can be prepared together. T-20 can be injected into the thigh, arm or abdomen. A different injection site should be used each day to reduce problems with injection site reactions.

Common side-effects: injection site reaction, possibly involving an itchy rash, swollen red or puffy skin, hardening of the skin, or cysts.

Rare side-effects: abscesses at the injection site. Headache, difficulty sleeping. Increased risk of bacterial pneumonia. Rare hypersensitivity reaction involving difficulty breathing, fever, chills, skin rash and low blood-pressure.

Resistance to T-20: test-tube studies suggest that resistance to T-20 does not cause resistance to the experimental entry inhibitor T-1249. People who are resistant to T-20 may still get some benefit from it.

Key drug interactions: no significant interactions recorded.

44 Other drugs

Immune-based therapies

In addition to antiretroviral therapies to combat HIV, treatments aimed at strengthening the immune system are currently being studied.

Interleukin-2 (IL-2) is a naturally occurring chemical in the immune system which stimulates CD4 cell production. A clinical trial called Esprit, which is investigating the long-term effects of interleukin-2 with anti-HIV drugs, is underway in many centres in the UK. For details ask your health care team or visit NAM's website *aidsmap.com*.

Summary

- Anti-HIV drugs prevent HIV from damaging your immune system, and so prevent ill health and prolong survival.
- The best time to begin anti-HIV drugs is not known. Decisions are guided by the CD4 count and viral load. It is currently recommended that treatment starts before the CD4 count falls below 200.
- Combinations of at least three anti-HIV drugs provide the best chance of reducing the amount of HIV in your blood to very low levels.
- Taking your anti-HIV drugs as prescribed is extremely important, as this will prolong the benefit you will get from them, and reduce the risk of resistance to the drugs developing.
- Tell a member of your HIV care team (doctor, nurse or pharmacist) if you are having problems with your anti-HIV drugs. Make sure that they know about any other medicines you are taking (including those bought from a chemist, herbal preparations and recreational drugs).
- Five classes of antiretroviral drugs are now available in the UK.

46 Glossary

AIDS Acquired Immune Deficiency Syndrome.

AIDS-defining illness One of a group of illnesses associated with AIDS. If you are HIV-positive and you have one of these illnesses, you are said to have AIDS. For example, PCP or Kaposi's sarcoma.

absorption The amount of drug that gets into the blood.

approved dosage An effective and safe dose that has been approved by drug licensing authorities.

blood disorders Refers to conditions such as anaemia (low red blood cells) which causes fatigue, and neutropenia (low white blood cells).

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

experimental dosage Dosage/s being tested in trials and not approved by drug licensing authorities.

GUM clinics Genito-urinary medicine or sexual health clinics.

lipodystrophy A change to the way the body stores, handles and distributes fat. A side-effect of anti-HIV drug treatment.

metabolic abnormalities Anti-HIV drugs, particularly protease inhibitors, are associated with irregularities in the body's processing of sugar and fat, resulting in increased levels of these substances in the blood.

pancreatitis Inflammation of the pancreas. A serious, possibly life-threatening condition.

PCP *Pneumocystis carinii pneumonia* – a type of pneumonia which is diagnostic of AIDS.

peripheral neuropathy Nerve damage which causes pins and needles, altered sensation and pain, usually in the hands and feet.

resistance A resistant HIV strain is one which is less susceptible to one or more anti-HIV drugs.

special access scheme Before a drug is fully approved by drug licensing authorities, a pharmaceutical company may make a new treatment available through a special access scheme. This is sometimes called named patient prescribing or expanded access.

Stevens-Johnson Syndrome A severe or even life-threatening allergic reaction.

viral load Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.

HIV & AIDS Helplines

National Sexual Health Helpline

telephone 0800 567123
opening hours daily, 24 hours

Terrence Higgins Trust Helpline

telephone 0845 1221 200
opening hours Monday-Friday, 10am-10pm
Saturday & Sunday, 12noon-6pm

HIV i-Base Treatment Phoneline

telephone 0808 800 6013
opening hours Monday-Wednesday,
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Drug Chart sixth edition 2005 (unless stated, drugs are reproduced actual size)

Protease inhibitors

NRTIs

NRTIs cont.

NNRTIs

Nucleotide analogue reverse transcriptase inhibitors

Fusion inhibitors