

Antiretroviral Treatment Protocol

Provincial Administration Western Cape

(Based on National Treatment Guidelines)

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SECTION 1: ADULTS

1. Goals of antiretroviral therapy

The goal of antiretroviral therapy is to decrease HIV related morbidity and mortality.

- The patient should experience fewer HIV related illnesses.
- The patient's CD4 count should rise and remain above the baseline count.
- The patient's viral load should become undetectable (<400 copies/ml) and remain undetectable on ARV therapy.

2. Selection of patients for antiretroviral therapy

2.1 Referral for antiretroviral therapy

Patients being considered for antiretroviral therapy will need to meet medical criteria before starting antiretroviral therapy. In addition, psychosocial criteria should be taken into account when referring a patient for antiretrovirals. Psychosocial criteria are **not** exclusion criteria, but identify factors that place the patient at risk for poor adherence.

It is important to consider both the medical and psychosocial criteria listed below when referring patients. Antiretroviral therapy should not be started before it is medically indicated. Commencing antiretroviral therapy in patients who are unlikely to take their medication reliably places them at risk of developing viral resistance, limiting their further treatment options. Resistant virus may infect other people, which will ultimately impact on the success of the programme. The psychosocial criteria listed below identify factors that make the patient at risk for poor adherence to therapy. These issues should be addressed before referral. Problems such as alcohol or other substance abuse and depression should be actively managed before considering a patient for antiretroviral therapy. Patients require education about their disease and counselling before treatment is commenced.

Medical criteria:

- WHO stage 4 disease. (Tuberculosis is not a criterion for initiating ART unless CD4 count < 200 cells/mm³). See Table 1 for WHO Staging **OR**
- WHO stage 1, 2 and 3 patients with CD4 count < 200 cells/mm³

Psychosocial criteria:

- Demonstrated reliability i.e. has attended three or more scheduled visits to an HIV clinic.
- No active alcohol or other substance abuse.
- No untreated active depression.
- Disclosure: It is strongly recommended that clients have disclosed their HIV status to at least one friend or family member **OR** have joined a support group.
- Insight: Clients need to have accepted their HIV positive status, and have insight into the consequences of HIV infection and the role of ARV treatment before commencing ARV therapy.

Other:

- Able to attend the antiretroviral centre on a regular basis (transport may need to be arranged for patients in rural areas or for those remote from the treatment site).

2.2 Referral process

- Patients in need of antiretroviral therapy will be referred to the nearest ARV centre to their local health facility.
- The referral process will be by referral letter (see Appendix 1). Facilities should refer people who are clinically appropriate and who meet the above criteria.

2.3 Patient selection

- The final decision to treat will be taken by the multidisciplinary team at the ARV centre who will initiate treatment.
- The team must make a global assessment of the patient, including both medical and psychosocial criteria. The criteria listed in 2.1 should guide the decision of the clinical team.
- If the patient does not yet fulfill clinical criteria they should be referred back to their clinic of origin for ongoing management. These patients should be referred back to the antiretroviral center if they fulfill clinical criteria in the future.
- A plan should be made, together with the referring clinic, to address any psychosocial issues identified during the selection process, which need management before antiretroviral commencement. This may include additional counselling to address issues of disclosure and support, referral for management of substance abuse or initiation of treatment for depression.
- The following factors are positive and negative predictors of adherence¹, and should be taken into account when selecting and managing patients.

Table 1: Factors influencing adherence

Factors	Promote Adherence	Reduce Adherence
Patient factors	Motivated patient Good understanding of HIV disease and therapy Education given in patient's home language prior to and during therapy Participation in a support group	Alcoholism Depression Poor understanding of the disease or therapy Non-disclosure of HIV status (to close family/friends)
<i>Disease factors</i>	Late or symptomatic HIV disease	Early, asymptomatic disease
<i>Therapy factors</i>	Small number of tablets Few adverse events	Large number of tablets Severe or ongoing minor adverse events

¹ Adapted from Wilson D et al. Oxford Handbook of HIV Medicine.

Table 2: World Health Organisation staging system

<p>Stage One</p> <ol style="list-style-type: none">1. Asymptomatic (ASY)2. Persistent generalised lymphadenopathy (PGL)3. Acute retroviral infection (seroconversion illness) (ARI)
<p>Stage Two</p> <ol style="list-style-type: none">4. Unintentional weight loss < 10% of body weight (WL4)5. Minor mucocutaneous (e.g. seborrhoea, prurigo, fungal-nail, oral ulcers, angular cheilitis) (MMC)6. Herpes zoster within the last five years (HZV)7. Recurrent upper respiratory tract infection (e.g. bacterial sinusitis) (URTI)
<p>Stage Three</p> <ol style="list-style-type: none">8. Unintentional weight loss > 10% of body weight (WL8)9. Chronic diarrhoea > one month (DIA)10. Prolonged fever > one month (PYR)11. Oral candidiasis (ORC)12. Oral hairy leukoplakia (HLP)13. Pulmonary TB within the last year (PTB)14. Severe bacterial infections (pneumonia, pyomyositis) (BAC)15. Vulvovaginal candidiasis > one month / poor response to therapy (VVC)
<p>Stage Four</p> <ol style="list-style-type: none">16. HIV wasting (8+9 or 10) (CAC)17. Pneumocystis carinii pneumonia (proven: PCP, presumptive: PPCP)18. CNS toxoplasmosis (TOXO)19. Cryptosporidiosis + diarrhoea > one month (CRS)20. Isosporiasis + diarrhoea (ISO)21. Cryptococcosis - non pulmonary (CRC)22. Cytomegalovirus infection other than liver, spleen or lymph node (CMV)23. Herpes simplex infection; visceral or > one month mucocutaneous (HSV)24. Progressive multifocal leucoencephalopathy (PML)25. Disseminated mycosis (MYC)26. Candida oesophageal / tracheal / pulmonary (OEC)27. Atypical mycobacteriosis disseminated (MOTT)28. Non-typhoidal Salmonella septicaemia (SAL)29. Extra-pulmonary tuberculosis (ETB)30. Lymphoma (LYM)31. Kaposi's sarcoma (KS)32. HIV encephalopathy (ADC)33. Invasive cervical carcinoma34. Recurrent pneumonia

2.3 Families

Patients who are referred for antiretroviral therapy should be encouraged to bring their sexual partner / spouse and children for voluntary counselling and testing. Family members must also be clinically staged and offered therapy when appropriate.

2.4 Reasons for deferring antiretroviral therapy

A patient may have therapy deferred (temporarily or permanently) due to:

- Not being “treatment ready” (see 3.1.4, page 6.)
- Being an unreliable clinic attendee
- Not fulfilling clinical criteria for antiretroviral therapy
- An acute opportunistic infection that requires immediate management
- Acute / uncontrolled depression
- Uncontrolled alcohol (or other substance) abuse

3. Process for initiation of antiretroviral treatment

3.1 Induction schedule

3.1.1 First screening visit (week –4:) 4 weeks before starting antiretroviral therapy

When the patient arrives with the referral letter from his/her local clinic:

1. Doctor or clinic nurse checks treatment qualification criteria.
2. Doctor makes a clinical assessment of the patient.
3. Patient attends an initial education session with the therapeutic counsellor.
4. Therapeutic counsellor delivers basic HIV and ARV information verbally and using pamphlets (Appendices 2 and 3).
5. Doctor and/or therapeutic counsellor discuss selection of treatment support person, and ask for that person to attend at the next visit if possible.
6. All patient contact details are recorded.
7. 28-day supply of co-trimoxazole is dispensed and the patient requested to bring the packet to the following 2 visits.

Patients who do not meet the treatment readiness criteria should be referred back to their local clinic with a detailed letter, including reason for deferment of antiretroviral treatment.

3.1.2 Home visit by therapeutic counsellor or treatment advocate

If the resources are available for the therapeutic counsellor or treatment advocate to make a home visit soon after the screening visit, this should be encouraged. This visit is useful to assess correct contact details, home circumstances, level of disclosure, and potential tablet storage place.

3.1.3 Consolidation of ARV Education Visit (Week –2) 2 weeks before starting antiretroviral therapy

This is the second clinic visit and occurs about 2 weeks after the screening visit. The patient has had time to consider the implications of ARV treatment. The following should be done:

1. The clinic nurse should take the baseline bloods: full blood count with differential, and ALT as per schedule (Table 2).
2. Count the co-trimoxazole tablets. If one tablet per day since the last visit has not been taken, the reasons should be elucidated. This can be valuable information regarding the patient's ability to understand instructions and adhere to them.
3. Patient attends a second education session with the therapeutic counsellor who clarifies all questions about HIV or treatment and reinforces adherence issues.
4. Ideally the patient should bring a support partner who should sit in on the second visit with the therapeutic counsellor.

3.1.4 Multidisciplinary team discussion

Before the next visit, the ARV clinic team should assess the patient's treatment readiness. All available information should be ready for the discussion (clinical assessment, CD4 count, viral load and safety blood results, results of 2 education sessions and co-trimoxazole count). A decision should be made about commencing treatment (see 2.3).

- If treatment is to be deferred, the patient should be referred back to their clinic of origin with a detailed letter.
- If the patient is not treatment ready, provide repeat counselling and education.
- Tuberculosis must be excluded before starting ARVs.

If 2 or more of the following are present, tuberculosis is likely:

- Observed weight loss of ≥ 1.5 -2 kg over the past 4 weeks
- Cough >2 weeks
- Night sweats > 2 weeks
- Fever > 2 weeks

Investigate these patients for tuberculosis **before** starting antiretrovirals.

- Patients who are acutely ill with an opportunistic infection should have this infection treated before initiating antiretroviral therapy.
- If the patient is treatment ready, drugs within schedule 1 should be selected for the patient to commence treatment in 2 weeks time.

Patients are 'treatment ready' when:

- They show an understanding of what can be expected on ARV treatment.
- They have an understanding of the possible side effects they may experience and know where to go in an emergency.
- They recognise the importance of daily adherence to therapy.
- They have disclosed to one friend or family member able to support them.

3.1.5 ARV commencement visit (Week 0)

At this visit the patient commences antiretroviral therapy. The doctor and therapeutic counsellor should reassess treatment readiness. The following should be done:

1. Second co-trimoxazole count – to confirm adherence over the past month.
2. A third, potentially brief, visit to the therapeutic counsellor to discuss final information and adherence issues.
3. The doctor should commence therapy with a detailed description of drug dosing using a treatment chart (Appendix 5) and have the patient explain the schedule to her/him.
4. The nurse should reinforce dosing details before the patient leaves the clinic and ensure that the instructions are clearly written on the drug container with a permanent marker.

3.1.6 Role of the pharmacist

Many antiretroviral sites will have access to a pharmacist. The role of the pharmacist should include:

- Drug accountability for the site (ordering and management of antiretroviral stock).
- Ensuring that the prescriptions are appropriate for a patient's needs by confirming the indication, safety & effectiveness of the antiretroviral and/or concomitant therapy.
- Dispensing of medication on the prescription of a person authorized to prescribe medicine.
- Supplying information & advice to patients with regard to medication, including side effects and dosing details.
- Determining patient adherence to the therapy, and, together with the clinical team, providing adherence support.

In sites without a pharmacist, the clinical team shares these responsibilities as in 3.1.1 to 3.1.5 above.

4 ARV treatment visits

4.1 Scheduled visits

Once treatment is commenced the visits follow as below:

1. Patients should be seen by the doctor at 4, 8 and 12 weeks and 3-monthly thereafter.
2. Patients on NVP should be seen by the nurse at 2 weeks (in addition to the visits above).
3. Patients attend monthly to collect medication and are seen by the professional nurse to monitor drug tolerance, adverse events and adherence. Drugs should be counted at each scheduled visit. Returns and drugs dispensed must be carefully recorded for adherence assessments.
4. Patients should visit the therapeutic counsellor monthly for 6 months and, at a minimum, quarterly thereafter.
5. Safety bloods are taken as per schedule. CD4 count and viral load are done 6-monthly.

Table 3: Time events schedule

C = counsellor; D=doctor; N=nurse

Assessment	Screening (Wk -4)	Education (Wk -2)	Commence ARV (week 0)	Week 2	Week 4	Week 8	Monthly	3 Monthly	6 Monthly
Education / Therapeutic counsellor visit	C	C	C		C	C	C	C	
Treatment readiness assessment		C and D	C and D						
History	D		D						
Physical exam	D		D		D	D		D	
Complete registers	N		N		N	N		N	
Safety bloods ^a		N ^a			N ^a	N ^a			N ^a
Additional safety bloods (NVP) ^b				N ^a					
Viral load		N							N
CD4 count		N							N
Adverse events					D	D	N		
Adherence check ^c		N	N		N	N	N	D	

a. For details of safety bloods see 9.2. Additional safety bloods will be required in pregnancy- see 7.3

b. For patients on NEVIRAPINE there will be an extra ALT taken at week.

c. Calculate monthly adherence = (tablets dispensed - tablets returned)/(tablets prescribed) e.g.(30 - 5)/28 = 25/28= 0.9 (90%)

4.2 Unscheduled visits

- Clinical judgement will be used to assess whether additional safety bloods are required if a patient presents with an adverse event.

- NO extra CD4 counts or viral loads should be done. The only exception is repeating the viral load 3 months after a previous viral load >5000 copies/ml.

5 Information for patients

5.1 Pre-treatment information

To supplement the information provided by health care workers, the patient should be provided with three information pamphlets in the appropriate language:

1. The HIV Information pamphlet (Appendix 2) – covers HIV basics such as the staging of disease, healthy eating, worrying symptoms.
2. ARV Information pamphlet (Appendix 3) – discusses the risks and benefits, adverse events and importance of adherence.
3. Treatment Chart (Appendix 4) - a simple description of their specific regimen and dosing.

5.2 Pre-treatment therapeutic counsellor discussions

The following topics must be covered in the three pre-treatment education sessions:

1. Repeat information on pamphlets – ensure a clear understanding of the progression of HIV disease and the benefit of ARV therapy.
2. Discuss the reasons for good adherence and elicit patient factors that may improve or hinder therapy.
3. Drug specifics (side effects, interactions, tablet numbers and size, storage, what to do if a dose is missed).
4. Emphasise importance of disclosure in maintaining adherence to therapy: to a treatment support person and to previous/present sexual partners.
5. Encourage participation in a support group.
6. Confidentiality issues: patient will be discussed within the team, but not outside the team.
7. Arrange home visit.

5.3 Pre-treatment doctor/professional nurse discussions

Before the patient is commenced on therapy:

1. Emphasise importance of adherence; and that tablet taking behaviour will be monitored.
2. Repeat drug and dosing specifics.
3. Explain possible reasons for therapy change or withdrawal (virological failure, repeated/prolonged non-adherence, serious adverse reaction).
4. Explain visit schedules for the future.

6 Treatment and prophylaxis of opportunistic infections (OIs)

- Management of TB will be done in coordination with the local TB clinics.
- Patients treated for tuberculosis may require a change in their antiretroviral treatment (see flowchart 3).

- Co-trimoxazole prophylaxis **must** be continued in all patients on antiretrovirals until the CD4 count is above 200 cells/mm³.
- Patients who have had cryptococcal meningitis **must** continue taking fluconazole prophylaxis until the CD4 count is above 200 cells/mm³.

7 Antiretroviral regimens

7.1 Antiretroviral naïve adult patients

7.1.1 First-line therapy – Schedule 1

Unless contraindicated, all patients will commence therapy on:

1. Stavudine (d4T) 40mg every 12 hours (or 30mg every 12 hours if <60kg), with
2. Lamivudine (3TC) 150mg every 12 hours, and
3. Efavirenz (EFV) 600mg at night (or 400mg if <40kg) **OR**
Nevirapine (NVP) 200mg daily for 2 weeks, followed by 200mg every 12 hours.

- Injectable contraception should be prescribed in addition to condoms for women of child bearing potential who are started on efavirenz. The antiretroviral clinic must check that contraceptive injections have been administered on time.
- If unable to guarantee contraception for women while on therapy, nevirapine will be substituted for efavirenz. Extra safety bloods will need to be taken as per Table 10.
- Patients may occasionally need to change a drug from the first-line regimen to one from the second-line regimen, because of a serious adverse reaction (e.g. severe rash on nevirapine, requiring a swap to lopinavir/ritonavir, severely symptomatic peripheral neuropathy on stavudine, requiring a swap to zidovudine). Swapping limits the patient's second-line treatment options. The decision to swap must be made by a doctor with antiretroviral experience.

7.1.2 Second-line therapy –Schedule 2

Patients who continue to fail virologically despite efforts to improve adherence (see section 10) may be changed to schedule 2. Before changing to schedule 2, the patient should go through the treatment readiness and education process again. Most patients will commence schedule 2 as follows:

1. Didanosine (ddI) 400mg once a day (250mg daily if <60kg).
2. Zidovudine (AZT) 300mg every 12 hours.
3. Lopinavir/ritonavir (LPV/r) 400/100mg every 12 hours.

- Didanosine must be taken alone, on an empty stomach, at least an hour before (or 2 hours after) a meal. Tablets should be dissolved in at least 30mL of water or clear apple juice. No other fruit juice may be used to dissolve the tablets.
- Patients should try to keep their lopinavir/ritonavir cool (<25 degrees Celsius).

There are currently no further treatment options available within the public sector for patients who fail second-line therapy

7.2 Antiretroviral therapy for non-naïve adults

Patients who have been exposed to antiretroviral therapy in the past need to be discussed with an antiretroviral expert **before** a treatment regimen is commenced. A regimen of 3 (preferably all new to the patient) ARVs should be created from the ARVs available (see schedule 1 and 2 above).

7.3 Pregnant women

7.3.1 Women who fall pregnant before starting antiretroviral therapy

Pregnant women with early stage HIV, or HIV disease not requiring ARV therapy according to this protocol, will follow the PMTCT protocol for the district.

Women who present with late stage HIV who require ARV therapy according to the clinical criteria above, will be commenced on first-line therapy:

1. Stavudine (d4T) 40mg every 12 hours (or 30mg every 12 hours if <60kg), with
 2. Lamivudine (3TC) 150mg every 12 hours, and
 3. Nevirapine 200mg daily for 2 weeks, followed by 200mg every 12 hours.
- Treatment should not be initiated until the end of the 1st trimester
 - Exception should be made for a woman with a CD4 <50 cells/mm³, or with serious HIV illness, where ARVs should be started as soon as the patient is treatment ready.
 - For patients presenting after the 1st trimester, treatment will be commenced within as short a time as possible, in order to maximise time on antiretroviral therapy prior to delivery. Education processes must be condensed into 2 weeks and continued into early therapy. Pre-treatment visits should be weekly rather than 2 weekly.
 - Antenatal care, PMTCT information and care of the baby after delivery must continue as per the PMTCT protocol for the district *in addition to* the ARV programme.

7.3.2 Women who fall pregnant on antiretroviral therapy

- Women who fall pregnant on efavirenz must be counselled about potential teratogenicity (myelomeningocele has been described in humans). If they decide to continue the pregnancy, efavirenz must be stopped and nevirapine started. All cases to be discussed with an antiretroviral specialist.
- Women who fall pregnant on stavudine, lamivudine and nevirapine should continue their antiretroviral therapy throughout pregnancy. ALTs should be performed monthly.
- Women who fall pregnant on second-line therapy (zidovudine, didanosine and lopinavir/ritonavir) should continue their antiretroviral therapy throughout pregnancy. Full blood count should be performed monthly.

7.4 Concomitant tuberculosis

Tuberculosis is a common co-morbid illness with HIV. There are 2 scenarios to consider:

1. Patient develops tuberculosis while on antiretroviral therapy:

Antiretroviral therapy should be continued throughout TB treatment, with changes to schedules and monitoring as follows:

- Schedule 1: A change to efavirenz is recommended for patients on nevirapine whenever possible. If this is not possible (eg intolerant of efavirenz or significant risk of falling pregnant), nevirapine may be continued in selected cases, with monthly ALT monitoring. Discuss these cases with an antiretroviral expert.
- Schedule 2: Lopinavir/ritonavir should change to saquinavir/ritonavir (dose: 400/400 mg every 12 hours). This should be continued until 1 month after completion of TB treatment, when saquinavir/ritonavir can be swapped back to lopinavir/ritonavir.

2. Patient presents with TB before commencing ARVs:

- If the patient has no history of WHO Stage 4 illness, and has a CD4 count of more than 200 cells/mm³, antiretroviral therapy is not yet needed. The need for antiretrovirals should be reassessed on completion of TB treatment.
- If the patient has a history of WHO Stage 4 illness and/or a CD4 count of less than 200 cells/mm³, complete 2 months of TB therapy before commencing ARVs.
- If the patient has a CD4 count of less than 50 cells/mm³ or other serious HIV related illness, make sure that the patient is tolerating TB treatment before initiating ARVs (complete at least 2 weeks of TB treatment before initiating ARVs). Patients in this group should be started on first-line therapy consisting of stavudine, lamivudine and efavirenz (nevirapine should generally be avoided because of limited evidence and danger of shared hepatotoxicity).

Table 4 Shared side effects of TB and antiretroviral therapy

Side effect	Antiretroviral	Treatment for tuberculosis
Nausea	didanosine, zidovudine, ritonavir, saquinavir	pyrazinamide
Hepatitis	nevirapine, efavirenz	rifampicin, isoniazid, pyrazinamide
Peripheral neuropathy	stavudine, didanosine	isoniazid
Rash	nevirapine, efavirenz	rifampicin, isoniazid, pyrazinamide

Patients should be pre-emptively counselled about the following:

- **Treatment for TB together with ARV therapy involves taking a large number of tablets and they may struggle with adherence.**
- **When antiretrovirals are commenced, the patient's TB symptoms may transiently worsen as part of immune reconstitution.**

7.5 Immune reconstitution

- Patients with advanced HIV disease, particularly those with a CD4 count of less than 50 cells/mm³ may become ill with an immune reconstitution illness during the first few weeks of antiretroviral therapy.
- Immune reconstitution illnesses occur when improving immune function unmasks a previously occult opportunistic infection (an infection that was present in the patient's body, but was not clinically evident).
- Tuberculosis is a common immune reconstitution illness in South Africa.
- An immune reconstitution illness is not indicative of drug failure or a drug side effect. It is not a reason to stop antiretroviral therapy, or to change the antiretroviral regimen.
- Opportunistic infections may present in atypical ways during immune reconstitution. An experienced HIV clinician should be consulted for advice regarding investigation and management.

Flowchart 1: First-line Treatment of Adults (Schedule 1)

Please note:
Patients who have been exposed to ARVs in the past need to be discussed with an ARV expert BEFORE a treatment regimen is commenced.

Men or women on
reliable contraception

1. stavudine (d4T) 40mg every 12 hours (or 30mg bd if <60kg)

+

2. lamivudine (3TC) 150mg every 12 hours

+

3. efavirenz (EFV) 600mg at night (or 400mg if <40kg)

Women who are unable to
guarantee reliable contraception
while on therapy

1. stavudine (d4T) 40mg every 12 hours (or 30mg bd if <60kg)

+

2. lamivudine (3TC) 150mg every 12 hours

+

3. nevirapine (NVP) 200mg daily for 2 weeks, followed by 200mg every 12 hours

Swapping drugs:

- Drugs should only be swapped if a potentially serious side-effect develops or adherence is compromised.
- Swaps must be made by a doctor trained in antiretroviral therapy.

Flowchart 2: Second-line Treatment of Adults

Patients who have experienced virological failure which does not improve with stepped up adherence support may be changed to second-line therapy:

- The patient's response to therapy will be monitored by viral load and CD4 count.
- The first assessment will be after 6 months.
- At each visit the patient's viral load will place them into one of the categories below. Their category will determine further outcome and programme response (See table below).

Viral load (VL)	Response
<400 copies/ml	6 monthly viral load monitoring continues Routine adherence support
400-5000 copies/ml	<p>Repeat viral load in six months</p> <ul style="list-style-type: none"> ● Begin step-up adherence package. Review at next 6-month viral load ● If <400, return to routine 6 monthly monitoring and adherence support ● If still between 400 and 5000, continue with step-up adherence package, repeat viral load at 6 months ● If >5000, despite stepped up adherence support, switch to second-line therapy
>5000 copies/ml	<p>Repeat viral load in 3 months</p> <ul style="list-style-type: none"> ● Begin step-up adherence package. Review at next 6-month viral load ● If <400, return to routine, 6 monthly monitoring and adherence support ● If still between 400 and 500, continue with step-up adherence package, repeat viral load again after a further 6 months. ● If >5000, despite stepped up adherence support, switch to second-line therapy

Second-line antiretroviral regimen (Schedule 2)

1. zidovudine (AZT) 300mg every 12 hours, with
2. didanosine (ddI) 400mg once a day (250mg daily if <60kg), taken alone, dissolved in water or clear apple juice, on an empty stomach, and
3. lopinavir/ritonavir (LPV/r) 400/100mg every 12 hours

Patients need to keep their lopinavir/ritonavir cool (<25 degrees Celsius).

Flowchart 3: How to Treat Adult Patients with Concomitant Tuberculosis

TB develops while on ART

TB infection is present before starting ART

ADULTS:

- Continue ARV therapy throughout TB treatment
- Patients on first-line therapy containing nevirapine should be swapped to efavirenz as follows:

First-line therapy:

1. Stavudine 40 mg (or 30mg if <60kgs) every 12 hours
+
 2. Lamivudine 150mg every 12 hours
+
 3. Efavirenz 600mg at night

- Second-line regimen needs to be changed to a regimen compatible with standard TB therapy as follows:

Second-line therapy:

1. zidovudine (AZT) 300mg every 12 hours
+
 2. didanosine (ddI) 400mg once a day (250mg daily if <60kg) on an empty stomach
+
 3. saquinavir/ritonavir 400/400mg every 12 hours

ADULTS:

CD4+ count > 200/µl (and no other HIV-related symptoms):

- Assess the need for ART after completing TB therapy, using CD4 and clinical criteria

CD4+ count < 200/µl:

- Delay ARVs until after 2-month intensive phase of TB therapy.
- Then start first line therapy, as below.

CD4+ count of < 50/µl or other serious HIV illness

- Introduce ART as soon as the patient is stabilized on TB therapy (no less than 2 weeks between starting TB therapy and starting ART).

First-line therapy:

1. Stavudine 40 mg (or 30mg if <60kgs) every 12 hours
+
 2. Lamivudine 150mg every 12 hours
+
 3. Efavirenz 600mg at night

Remember:

Patients on TB medication and ARVs are taking a large number of tablets
- do pre-emptive counselling to improve adherence

Flowchart 4: How To Treat Pregnant Women

Pregnant women with early stage HIV, or HIV not requiring ARV therapy according to this protocol

Follow the PMTCT protocol for the district

Pregnant women who present with late stage HIV who require ARV therapy according to clinical criteria

Commence on first -line treatment:

1. stavudine (D4T) 40 mg every 12 hours (or 30mg every 12 hours if < 60kg)
+
2. lamivudine (3TC) 150mg every 12 hours
+
3. nevirapine 200mg daily for 2 weeks, followed by 200mg every 12 hours

Points to note:

- Do not initiate treatment in the first trimester, except in women with CD4 <200 or serious HIV related illness
- Start women presenting after the first trimester on ARVs as soon as possible, in order to maximise time on antiretroviral therapy before delivery
- Treatment-preparedness and education processes must be condensed into 2 weeks
- Antenatal care, MTCT information and follow-up of the baby must continue as per the district protocol, in addition to the ARV programme.

Women who fall pregnant on ARV therapy

Women on efavirenz:

- Counsel about possible teratogenicity
- If pregnancy is continued, stop efavirenz and start nevirapine
- Discuss with ARV specialist

Women on D4T + 3TC + nevirapine:

- Continue ARVs
- ALTs monthly

Women on AZT + ddI + lopinavir/ritonavir:

- Continue ARVs
- Full blood count monthly

8 Adverse reactions

8.1 Grading of adverse reactions

Table 5: Grading the severity of adverse reactions (ACTG)

LABORATORY TEST ABNORMALITIES				
ITEM	GRADE 1 TOXICITY	GRADE 2 TOXICITY	GRADE 3 TOXICITY	GRADE 4 TOXICITY
Hemoglobin	8.0-9.4 g/dL	7.0-7.9 g/dL	6.5-6.9 g/dL	<6.5 g/dL
Absolute Neutrophil Count	1-1.5 X 10 ⁹ /L	0.75-0.99 X 10 ⁹ /L	0.5-0.749X 10 ⁹ /L	<0.5X 10 ⁹ /L
ALT (SGPT)	1.25-2.5 X upper normal limit	>2.5-5 X upper normal limit	>5.0-10 X upper normal limit	>10 X upper normal limit
Triglycerides*	3-4.51 mmol/L	4.52-8.48 mmol/L	8.49-13.56 mmol/L	>13.56 mmol/L
Cholesterol**	>1.0-1.3 X upper normal limit	>1.3-1.6 X upper normal limit	>1.6-2.0 X upper normal limit	>2.0 X upper normal limit
CLINICAL ADVERSE EVENTS				
ITEM	GRADE 1 TOXICITY	GRADE 2 TOXICITY	GRADE 3 TOXICITY	GRADE 4 TOXICITY
Paresthesia (burning, tingling, etc)	mild discomfort; no treatment required	moderate discomfort; non-narcotic analgesia required	severe discomfort; OR narcotic analgesia required with symptomatic improvement	incapacitating; OR not responsive to narcotic analgesia
Neuro-sensory	Mild impairment (decreased sensation, e.g., vibratory, pinprick, hot/cold in great toes) in focal area or symmetrical distribution	Mod impairment (mod decrease in sensation, e.g., vibratory, pinprick, hot/cold to ankles) and/or joint position or mild impairment that is not symmetrical	severe impairment (decrease or loss of sensation to knees or wrists) or loss of sensation of at least mod degree in multiple different body areas (i.e., upper and lower extremities)	sensory loss involves limbs and trunk.
Cutaneous / Rash / Dermatitis*	erythema, pruritus	diffuse, maculopapular rash, OR dry desquamation	vesiculation, OR moist desquamation, OR ulceration	exfoliative dermatitis, OR mucous membrane involvement, OR erythema, multiforme OR suspected Stevens-Johnson OR necrosis requiring surgery

Adverse reactions will be graded according to the AIDS Clinical Trial Group (ACTG) grading.

- Grades 1 and 2 – client remains on therapy. Repeat the test. Reassess clinically within 2 weeks.
- Grade 3 – test should be repeated in 1 week and if still Grade 3, stop ALL antiretroviral drugs and seek expert medical advice.
- Grade 4 – Stop all drugs immediately and seek specialist advice. If the patient restarts therapy after the event has resolved, and the same grade 4 event recurs, appropriate changes or

withdrawal of antiretroviral therapy may need to be made. Decisions should be made on an individual basis, and discussed with experts as required.

A rash in a patient on nevirapine with mucosal involvement OR associated with fever / systemic symptoms / derangement in liver functions should be treated as a Grade 4 toxicity. All antiretrovirals should be stopped immediately. Patients at primary care should be referred to a specialist for advice regarding restarting antiretrovirals. The patient should never be rechallenged with nevirapine.

8.2 Important adverse reactions

Table 6: Important ARV adverse reactions

Antiretroviral	Adverse Reactions
Didanosine (ddI)	Pancreatitis Peripheral neuropathy GIT effects (bloating, flatulence, nausea, diarrhoea) Lactic acidosis
Efavirenz (EFV)	CNS disturbances (dysphoria, vivid dreams, distractedness, dizziness) GIT symptoms Skin rash <i>Congenital anomalies-Avoid during pregnancy</i>
Lamivudine (3TC)	Diarrhoea Pancreatitis Anaemia
Lopinavir/Ritonavir	GIT symptoms Lipid abnormalities Lipodystrophic changes
Nevirapine (NVP)	Skin rash (16%) Nausea Vomiting Hepatitis (can be fatal)
Ritonavir	Bad taste GIT symptoms Raised liver enzymes Lipodystrophic changes
Saquinavir	GIT side effects Headache Raised liver enzymes Lipodystrophic changes
Stavudine (d4T)	Peripheral neuropathy Hepatic steatosis Lactic acidosis
Zidovudine (AZT)	Bone marrow suppression (anaemia, neutropenia) GIT symptoms Myopathy Lactic acidosis

Please note: Other adverse reactions not listed on this table may occur.

8.3 Management of specific adverse reactions:

Nausea

- Nausea due to antiretroviral medication must be actively managed, or adherence will suffer.
- Metoclopramide 10mg, taken half an hour before the antiretroviral dose, may be helpful. Metoclopramide 10mg can be taken up to 3 times daily.
- If the nausea does not settle on metoclopramide, refer for expert advice.

Rashes on first-line therapy

- Both nevirapine and efavirenz may cause skin reactions. This usually occurs within the first 2 months of treatment.
- Enquire about systemic symptoms, and check the temperature in any patient presenting with a rash.
- Liver functions should be checked.
- If the patient has a fever, is systemically unwell, has a severe rash involving mucosal surfaces, or has abnormal liver functions ALL antiretroviral medication must be stopped **immediately**, and expert help sought.

Abdominal pain

- Abdominal pain in a patient on antiretrovirals can be caused by a number of serious problems, and should **never** be ignored.
- Important causes include pancreatitis, hepatitis, hyperlactataemia (increased serum lactate) and disseminated tuberculosis.
- Recommended investigations: full liver functions, amylase, and serum lactate.
- Seek expert help if you are unsure of the cause of the pain.

Hyperlactataemia and lactic acidosis

- Asymptomatic elevation of lactate is common in patients taking antiretrovirals (up to 20% per year). Routine monitoring of lactate is not recommended if the patient is asymptomatic.
- Patients on ARVs can occasionally develop symptomatic hyperlactataemia (1-2% per year), and, more rarely, lactic acidosis (0.1-0.2% per year).
- Risk factors for lactic acidosis include female gender, obesity, prolonged antiretroviral therapy, and excellent adherence with therapy.
- Symptoms are non-specific, and include nausea, vomiting, abdominal pain, shortness of breath, fatigue and weight loss. A mild transaminitis together with any of the above symptoms should also raise suspicions.
- In patients with suspicious symptoms or biochemistry, measure the venous lactate level (normal level is less than 2 mmol/L). A specimen for measurement of venous lactate needs to be taken fasting, without a cuff, and must be transported to the laboratory on ice within 15 minutes. Refer patients for lactate testing if these requirements for sampling cannot be met at your site.

- **Respond as follows:**

- Lactate 2-5 mmol/L: monitor monthly, and be alert for clinical symptoms and signs described above.
 - Lactate 5-10 mmol/L without symptoms: monitor closely. Seek expert advice.
 - Lactate 5-10 mmol/L with symptoms: STOP all antiretroviral therapy and seek urgent expert help. Other causes of raised lactate e.g. sepsis, renal failure and diabetic ketoacidosis, must be excluded.
 - Lactate > 10 mmol/L: STOP all antiretrovirals immediately and seek urgent expert help (80% mortality in case series).
 - Metabolic acidosis with raised lactate- STOP all antiretroviral therapy and seek urgent expert help.
- After recovery, seek expert advice regarding antiretroviral selection. Stavudine and didanosine should be avoided.

Lipodystrophy

- Antiretrovirals (particularly NRTIs and protease inhibitors) may cause abnormal fat distribution.
- Features include increased abdominal girth, breast enlargement, buffalo hump and peripheral fat wasting.
- Patients may find these changes disfiguring, which may impact on adherence.
- These changes may have to be tolerated, or the antiretroviral therapy stopped.
- Swapping or stopping drugs does not always improve the changes.
- Together with the physical changes, patients may become hyperlipidaemic and develop impaired glucose tolerance. Monitor for these adverse effects.

Hyperlipidaemia

- Patients on lopinavir/ritonavir who develop hyperlipidaemia should be counselled about lifestyle modification (weight loss if obese, increasing exercise, stopping smoking, reducing cholesterol and saturated fat intake) and referred to a dietician, if available, for dietary advice.
- Severe hyperlipidaemia may require drug management. If triglyceride > 5.6mmol after dietary changes or LDL > 4.9 mmol (LDL > 3.4 mmol if 2 or more other ischaemic heart disease risk factors), refer the patient for further management (fibrates or atorvastatin).

Zidovudine-related anaemia or neutropaenia.

- If the patient develops a grade 3 or 4 anaemia or neutropaenia on zidovudine, the dose can be reduced to 250mg 12-hourly.
- If the anaemia or neutropaenia does not improve after dose adjustment, then zidovudine may have to be replaced with stavudine (seek expert advice).

8.4 Substitutes for intolerance

- All switches should be made by a doctor trained in antiretroviral therapy.

Table 7: Recommended substitutions for specific side effects (grade 3 or 4 toxicity)

Regimen	Toxicity	Drug substitution
d4T/3TC/NVP	<ul style="list-style-type: none"> • d4T-related neuropathy or pancreatitis • NVP-related severe hepatotoxicity • NVP-related severe rash (but not life threatening) • NVP-related life threatening rash (Stevens-Johnson syndrome) 	<ul style="list-style-type: none"> • Switch d4T → AZT • Switch NVP → EFZ (except in pregnancy) • Switch NVP → EFZ • Switch NVP → lopinavir/ritonavir
d4T/3TC/EFZ	<ul style="list-style-type: none"> • d4T-related neuropathy or pancreatitis • EFZ-related persistent CNS toxicity 	<ul style="list-style-type: none"> • Switch d4T → AZT • Switch EFZ → NVP
AZT/ ddI/ lopinavir/ritonavir	<ul style="list-style-type: none"> • AZT related anaemia or neutropenia • ddI related GIT side effects • ddI related pancreatitis or hepatitis • LPV/r related GIT symptoms • LPV/r related hypercholesterolaemia • Lipodystrophy 	<ul style="list-style-type: none"> • Switch AZT → d4T • Switch ddI for enteric coated ddI • Consult expert • Consult expert • Consult expert • Consult expert

8.5 Drug interactions

Protease inhibitors (eg lopinavir/ritonavir, ritonavir and saquinavir) and non-nucleoside reverse transcriptase inhibitors (efavirenz and nevirapine) can interact with a number of other drugs, through changes in drug metabolism in the liver. The following are examples of drugs that should be used with caution (requiring dosage adjustment) or should be avoided, when administered with efavirenz, nevirapine, lopinavir/ritonavir or all 3 drugs. Seek expert advice if your patient is taking one of these drug combinations.

Table 8: Drug interactions

Interacting drug	Lopinavir/ritonavir*	Efavirenz	Nevirapine
Amitriptyline	May need dose adjustment	–	–
Atenolol	May need dose adjustment	–	–
Atorvastatin	May need dose adjustment	May need dose adjustment	May need dose adjustment
Azithromycin	May need dose adjustment	May need dose adjustment	–
Carbamazepine	AVOID this combination	May need dose adjustment	May need dose adjustment
Chlorpromazine	May need dose adjustment	–	–
Combined oral contraceptive	May need dose adjustment	May need dose adjustment	May need dose adjustment
Diazepam	AVOID this combination	May need dose adjustment	May need dose adjustment
Ergotamine	AVOID this combination	AVOID this combination	May need dose adjustment
Erythromycin	May need dose adjustment	–	–
Fluconazole	–	–	May need dose adjustment
Fluoxetine	May need dose adjustment	–	–
Haloperidol	May need dose adjustment	–	–
Metoclopramide	May need dose adjustment	–	–
Metronidazole	May need dose adjustment	–	–
Nifedipine	May need dose adjustment	May need dose adjustment	May need dose adjustment
Phenytoin	May need dose adjustment	May need dose adjustment	May need dose adjustment
Simvastatin	AVOID this combination	May need dose adjustment	May need dose adjustment
St John's Wort	AVOID this combination	AVOID this combination	AVOID this combination
Theophylline	May need dose adjustment	–	–
Valproate	May need dose adjustment	May need dose adjustment	May need dose adjustment
Warfarin	May need dose adjustment	May need dose adjustment	May need dose adjustment

* All of these interactions also apply to ritonavir when used in combination with saquinavir.

- There is the potential for drug interactions with many other medications, including over-the-counter and traditional remedies.
- Contact the Medicines Information Centre, UCT for advice regarding potential interactions, and recommendations for dosage adjustment. Phone 021 406-6782.

8.6 Treatment interruptions

- If ARV treatment is interrupted, ALL antiretroviral medication must be stopped together.
- Never stop only one antiretroviral.
- Do not interrupt therapy unnecessarily.

8.7 Reporting of adverse events

Report serious or unexpected suspected adverse reactions or suspected drug interactions to the National Adverse Drug Event Monitoring Centre. Phone (021) 447-1618 to report.

9 Monitoring of efficacy and safety

Monitoring of both efficacy and safety is essential to:

- Prevent the development of resistance.
- Prevent drug failure.
- Limit the occurrence of serious and potentially fatal adverse reactions.

9.1 Efficacy

- Viral load when initiating first line regimen should be done prior to initiation of therapy and every 6 months thereafter.
- CD4 count should be done 6 monthly.

9.2 Safety

Table 9: Recommended safety monitoring

Antiretroviral	Monitoring recommended
Didanosine	Clinical
Efavirenz	Clinical
Lamivudine	Clinical
Lopinavir/ritonavir	Fasting cholesterol and triglyceride at baseline, 6 months and thereafter every 12 months. Fasting glucose every 12 months
Nevirapine	ALT at baseline and at week 2,4, and 8 and thereafter every 6 months (taken with CD4 and viral load) or with symptoms
Ritonavir	Fasting cholesterol and triglyceride at baseline, 6 months and thereafter every 12 months.
Stavudine	Clinical
Zidovudine	FBC with white cell diff. count at baseline, then monthly for 3 months, then 6 monthly (with CD4 and viral load) thereafter

Table 10: Summary of Adult ARV Regimens and routine monitoring during treatment

Regimen	Test	Frequency
d4T / 3TC / NVP	<ul style="list-style-type: none"> • CD4 • VL • ALT 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, week 2, 4 and 8, thereafter 6 monthly
d4T / 3TC / efavirenz	<ul style="list-style-type: none"> • CD4 • VL 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly
AZT / ddi / lopinavir / ritonavir	<ul style="list-style-type: none"> • CD4 • VL • FBC • Fasting cholesterol and triglyceride • Fasting glucose 	<ul style="list-style-type: none"> • Staging, 6-monthly • 6 monthly • baseline, then monthly for 3 months, then 6 monthly (with CD4 and viral load) thereafter • baseline, 6 months and thereafter every 12 months. • Every 12 months

- **Staging** = initial testing for all patients when being referred for antiretroviral therapy
- **Baseline** = testing for ARV eligible patients, at initiation of ARVs

10 Adherence to ARVs.

- Success of antiretroviral therapy hinges on tablet taking behaviour.
- Ideal adherence means a patient must take more than 95% of their doses (i.e. missing less than 3 doses in a month).
- If a patient is taking fewer than 95% of their doses, they are at risk for developing viral resistance and ultimately virological failure.

Patients taking <80% of their doses are unlikely to have any durable virological suppression and should be targeted urgently for adherence improvement.

10.1 Basic package at initiation

Pre-treatment:

- Pre-treatment information and education as per visit schedule.
- Patient is introduced to therapeutic counsellor and treatment advocate, if available, and home visit is arranged.

- Co-trimoxazole count for 1 month prior to commencing therapy. (This is not to be used to exclude people from ARV treatment. It is meant to reinforce daily medication taking behaviour from the outset, and identify potential problems before starting ARV s).

On treatment:

At each visit:

- ARV pill-returns count (% doses missed). Adherence goal is >95% doses taken. Patients with adherence <80% require increased adherence support (see below).
- Tablet count must be done before the patient sees the doctor, and the count reviewed by the doctor at every visit.
- Missed/late clinic visits should trigger concerns about adherence.
- Routine adherence discussion/education with counsellor. This should be an open-ended discussion, with time for questions and repetition.
- Feedback from therapeutic counsellors to rest of team.
- Encourage participation in a support group.
- Continue monthly visit with therapeutic counsellors for first three months and quarterly thereafter.
- Arrange regular community visit by treatment advocate.

10.2 Step-up adherence package for people with reduced adherence or virological failure

Adherence assessment <80% at any visit, with or without viral or clinical failure (described in Table 5).

- Re-educate about importance of adherence. Re-emphasise long-term benefits.
- Consider use of pillbox and/or daily dosing diary.
- Insist on participation in a support group.
- Check family situation (through social worker and therapeutic counsellor).
- Increase home visits by therapeutic counsellors / treatment advocates to weekly at a minimum (spot pill counts to be done at home).
- Consider directly observed therapy.

11 Treatment failure

Patient's response to therapy will be monitored by viral load and CD4 count. The first assessment will be after 6 months. At each visit the patient's viral load will place them into one of the categories below. Their category will determine further outcome and programme response. See Table 10.

Table 11: Response to changes in viral load

Viral load (VL)	Response
<400 copies/ml	6 monthly monitoring continues Routine adherence support
400-5000 copies/ml	Repeat viral load in 6 months Begin step-up adherence package. Review at next 6-month viral load and respond as follows: <ul style="list-style-type: none"> • If <400: return to routine 6 monthly monitoring and adherence support • If still between 400 and 5000: continue with step-up adherence package, repeat viral load at 6 months. • If >5000, despite stepped up adherence support, switch to schedule 2
>5000 copies/ml	Repeat VL in 3 months . Begin step-up adherence package. Review at 3 month viral load and respond as follows: <ul style="list-style-type: none"> • If <400: return to routine 6 monthly monitoring and adherence support • If viral load has dropped to between 400 and 5000: continue with step-up adherence package, repeat viral load at 6 months. • If >5000, despite stepped up adherence support, switch to schedule 2

Once receiving stepped up adherence support, a patient may NOT return to routine monitoring without the adherence situation being discussed by the doctor – nurse - therapeutic counsellor team.

- Patients on second-line therapy (schedule 2) who begin to fail virologically should receive increased adherence support, as described above.
- If they continue to fail virologically, despite increased adherence support, their ARVs should be continued until they cease to derive clinical benefit from treatment.
- If the patient experiences an AIDS defining (WHO stage 4) illness on second-line therapy, expert opinion should be sought regarding stopping antiretroviral therapy, and moving on to palliative care.

SECTION 2: PAEDIATRICS

1. Goals of antiretroviral therapy

The goal of antiretroviral therapy for children is to decrease HIV related morbidity and mortality.

- The child's CD4 count should rise and remain above the baseline count.
- The child's viral load should become undetectable (<400 copies/ml) and remain undetectable on ARV therapy.
- In some children, a suppressed though detectable viral load, with sustained elevation in CD4 count and absence of intercurrent and/or opportunistic infection, may be the best achievable goal.

2. Selection of patients for antiretroviral therapy

2.1 Criteria for commencing antiretroviral therapy in children

Children being considered for antiretroviral therapy will need to meet both medical and psychosocial criteria before starting therapy.

Medical criteria:

- Recurrent hospitalisations (> 2 admissions per year) for HIV-related disease, or prolonged hospitalisation (> 4 weeks) OR
- Modified WHO stage 2 and 3 patients OR
- For modified stage 1 disease - CD4 count < 20% if < 18 months old or < 15% if > 18 months old.
(See Table 11)

Psychosocial criteria:

- An identifiable adult who is able to administer medication.
- Demonstrated reliability in adult caregiver i.e. has attended three or more scheduled visits to an HIV clinic. Immunization record of child is up-to-date.

Previous record of adherence to nutritional supplements or other chronic care regimens such as TB drugs may help to identify children who are at risk of poor adherence.

Other

- Able to attend the antiretroviral centre on a regular basis (transport may need to be arranged for patients in rural areas or for those remote from the treatment site).

Table 12: Modified World Health Organisation paediatric HIV/AIDS classification

<p>Stage One</p> <ol style="list-style-type: none"> 1. Asymptomatic 2. Generalized lymphadenopathy 3. Hepatomegaly 4. Splenomegaly 5. Hepatosplenomegaly
<p>Stage Two</p> <ol style="list-style-type: none"> 6. Unexplained chronic diarrhoea (≥ 2 weeks) 7. Failure to thrive <ul style="list-style-type: none"> • 60 - 80% expected body weight • Not responding to nutritional rehabilitation or anti-TB therapy (if clinically indicated). Other correctable causes excluded 8. Recurrent or severe bacterial infection (≥ 2 episodes pneumonia or 1 episode meningitis) 9. Oral candidiasis beyond neonatal period <ul style="list-style-type: none"> • Severe persistent or recurrent, not responding to topical therapy 10. Persistent fever (≥ 2 weeks) 11. Haematological <ul style="list-style-type: none"> • Thrombocytopenia (platelet count $< 40\,000 \times 10^9/l$) not responding to prednisone 2mg/kg/day after 2 weeks • Neutropaenia (neutrophil count $< 500 \times 10^9/l$) not responding to switch from cotrimoxazole to dapsone 12. Severe lymphoid interstitial pneumonitis with clubbing 13. ≥ 2 episodes Zoster or severe herpetic disease 14. Otorrhoea > 6 weeks 15. Single episode of proven or probable tuberculosis
<p>Stage Three</p> <ol style="list-style-type: none"> 16. AIDS opportunistic infection 17. Severe failure to thrive <ul style="list-style-type: none"> • $< 60\%$ expected body weight • Not responding to nutritional rehabilitation or TB therapy if clinically indicated 18. Progressive encephalopathy 19. Recurrent septicaemia (≥ 2 episodes) 20. Bronchiectasis (clubbing and persistent nocturnal cough) 21. Cardiomyopathy 22. Progressive nephropathy 23. Candidiasis (oesophageal or pulmonary). 24. Disseminated fungal infection (Coccidioidomycosis, Cryptococcosis, Histoplasmosis) 25. Disseminated mycobacterial infection (M tuberculosis, BCG, avium-intracellulare, Kansaii) 26. CMV disease with onset at age > 1 month (at site other than lymph nodes, spleen, liver). 27. HSV causing mucocutaneous ulcer persisting > 1 month, or bronchitis, oesophagitis, pneumonitis, oesophagitis in a child older > 1 month. 28. Pneumocystis carinii Pneumonia (PCP) 29. Progressive multifocal leukoencephalopathy. 30. Recurrent pulmonary tuberculosis

2.2 Referral process

The clinical team at the referral site should make the decision to refer for treatment. The referral team should include clinical, nursing, counselling staff and the child's mother or other caretaker.

- Children in need of antiretroviral therapy will be referred to the nearest ARV centre from their local health facility.
- The referral process will be by referral letter. Facilities should refer children who are clinically appropriate and who meet the above criteria.
- The final decision to treat will be taken at the ARV centre after further clinical and social assessment.

3. Process for initiation of antiretroviral treatment

3.1 Induction schedule

3.1.1 First screening visit (week – 4 or 4 weeks before starting antiretroviral therapy):

When the child arrives with the referral letter:

1. Complete history and clinical evaluation including weight and height.
2. Update growth chart.
3. Calculate surface area (See paediatric dosing schedule – Appendix 5).
4. Ensure that TB adequately excluded:
 - a. History of TB contact
 - b. Chest radiograph
 - c. Gastric aspirates or induced sputum if abnormal chest X ray
 - d. Mantoux test
 - e. Abdominal ultrasound (if clinically indicated and possible) for lymphadenopathy
5. Name the caregiver responsible for medication and make sure that this person is present during all discussion regarding antiretroviral therapy.
6. Explain the importance of adherence as well as tools to help improve adherence including the use of pillboxes, syringes, diary cards as well as the bringing back of all empty containers and unused drugs for all follow up visits.
7. Explain the side effects of ARVs with emphasis on problems associated with the chosen drug regimen.
8. Exact drug schedule for the child explained to the guardian.
9. Baseline investigations according to table 14.

3.1.2 Treatment visit 1 (Week 0):

1. Complete history and clinical evaluation including weight and height.
2. Update growth chart.
3. Calculate surface area (See paediatric dosing schedule – Appendix 5).
4. Check baseline blood results (taken at first screening visit).

5. Explain the importance of adherence and illustrate tools to help improve adherence including the use of pill boxes, syringes, diary cards as well as the bringing back of all empty containers and unused drugs to all follow up visits.
6. Explain possible side effects of ARVs with emphasis on the problems associated with the chosen drug regimen.
7. Explain drug schedule for the child to the guardian, using the diary card.
8. Commence ARVs.
9. Prescribe medication for 2 weeks, calculating total volume of medicine and number of units required.
10. Issue pillboxes, syringes and diary cards.
11. Arrange adherence phone call in 1 week (if possible).
12. Arrange follow up visit after 2 weeks.

4. ARV treatment visits

4.1 Scheduled visits

4.1.1 Treatment visit 2 (2 weeks after therapy initiation):

1. Complete history and clinical evaluation including weight and height.
2. Update growth chart.
3. Calculate surface area (See paediatric dosing schedule – Appendix 5.)
4. Adherence assessment (3 day recall).
5. Reconcile returned empty containers with volume of medication prescribed for prior interval.
6. Look for signs of toxicity (e.g. right upper quadrant tenderness, pallor, rash).
7. Explain exact drug schedule for the child to the guardian, using the diary card.
8. Issue medication for 2 weeks calculating total volume of medicine and number of units required.
9. Issue pillboxes, syringes and diary cards where needed.
10. Arrange follow up visit after 2 weeks.

4.1.2 Treatment visit 2 (4 weeks after initiation of treatment):

1. Complete history and clinical evaluation including weight and height.
2. Update growth chart.
3. Calculate surface area (See paediatric dosing schedule – Appendix 5).
4. Adherence assessment (3 day recall).
5. Reconcile returned empty containers with volume of medication prescribed for prior interval.
6. Look for signs of toxicity (e.g. right upper quadrant tenderness, pallor, rash).
7. Explain exact drug schedule for the child to the guardian, using diary card.
8. Adjust drug schedule if needed (e.g. nevirapine).
9. Do safety investigations according to table 14.
10. Issue medication for 4 weeks, calculating total volume of medicine and number of units required.

11. Issue pill boxes, syringes and diary cards where needed.
12. Arrange follow up visit after 4 weeks.

4.1.3 Treatment visit 3 (8 weeks after initiating therapy):

1. Complete history and clinical evaluation including weight and height.
2. Update growth chart.
3. Calculate surface area (See paediatric dosing schedule – Appendix 5).
4. Adherence assessment.
5. Reconcile returned empties with volume of drug issued at last visit.
6. Look for signs of toxicity (e.g. right upper quadrant tenderness).
7. Do safety investigations according to table 14.
8. Explain exact drug schedule for the child to the guardian.
9. Issue medication for 4 weeks calculating total volume of medicine and number of units required.
10. Enquire about full units of medication left over at home, include these in assessment of adherence and calculation of number of units required for the next interval.
11. Issue pillboxes, syringes and diary cards where needed.
12. Arrange follow up visit after 4 weeks.

Schedule following visits at monthly intervals until week 12 of therapy, then consider 3 monthly visits

At each subsequent visit

- Repeat measures 1 to 12 from treatment visit 3 above. (See 4.1.3 above).
- When 3 monthly visits are initiated, make sure the guardian understands what it means to collect repeat medicines at **monthly** intervals until the next visit.
- At each visit, enquire about surplus units of medication at home and include these in the calculation of volumes to be issued.

5. Paediatric antiretroviral regimens

See Appendix 5 for dosing schedule

Remember to recalculate doses according to body weight or body surface area at every three monthly visit

5.1 First line therapy – Schedule 1

Unless contraindicated, all children will commence therapy on:

Children < 6 months of age:

If fridge available:

1. Stavudine (d4T), with
2. Lamivudine (3TC), and
3. Ritonavir

If no fridge available:

1. Zidovudine (AZT), with
2. Lamivudine (3TC), and
3. Ritonavir

Children > 6 months of age

If fridge available:

1. Stavudine (d4T), with
2. Lamivudine (3TC), and
3. Lopinavir/ritonavir

If no fridge available:

1. Zidovudine (AZT), with
2. Lamivudine (3TC), and
3. Lopinavir/ritonavir

- Switch to tablets or capsules from syrups or solutions as soon as possible.
- Children may occasionally need to change a drug from the first-line regimen to one from the second-line regimen, because of intolerance or a serious adverse reaction. Swapping limits the patient's second-line treatment options. The decision to swap must be made by a doctor with antiretroviral experience.
- If intolerance develops to ritonavir or lopinavir/ritonavir, switch to nelfinavir.
- Lopinavir/ritonavir needs to be kept cool (< 25 degrees Celsius).

5.2 Second-line therapy – Schedule 2

Consider a move to second line therapy under the following conditions:

Table 13: Reasons to move to second-line antiretroviral therapy in children

Virological	Clinical	Immunological
<p>Rebound of viral load to baseline</p> <p>A detectable viral load may be tolerated in children, providing that growth and elevated CD4 count are sustained</p>	<p>Persistent oral thrush, which is refractory to treatment</p> <p>New evidence of stage III disease</p> <p><i>Note: Short intercurrent episodes of pneumonia, lower respiratory tract infection (LRTI) and gastroenteritis should not be regarded as clinical failure. Presentation with TB while on first-line therapy is NOT an indication to switch to second-line therapy</i></p> <p><i>TB can present as progression to stage III disease and must be excluded before the decision is made to switch to second-line</i></p>	<p>A persistent decline in the CD4% over 2 months in the absence of TB</p> <p><i>Note: The CD4% should NOT be measured during an intercurrent infection – but preferably a month post resolution.</i></p> <p><i>If there is a modest decline in CD4% (< 5%) and if no failure to thrive, do not change medication, but monitor closely</i></p>

Procedure for introduction of second-line therapy:

- Do not rush into second-line therapy.
- First check adherence; if it is not possible to improve adherence, attempt directly observed therapy (DOT) with a health care worker or trusted ‘other’ family member or friend.
- Ensure second-line therapy does not include any drugs used in first –line therapy.

Most children will commence schedule 2 as follows:

Children < 3 years old or < 10 kg:

If fridge available:

1. Didanosine (ddl), with
2. Zidovudine (AZT), and
3. Nevirapine

If no fridge available (and child previously on zidovudine as part of first-line therapy):

1. Didanosine (ddl) tablets, with
2. Abacavir (ABC), and
3. Nevirapine

Children > 3 years old and > 10 kg:

If fridge available:

1. Didanosine (ddl), with
2. Zidovudine (AZT), and
3. Efavirenz (EFV)

If no fridge available:

1. Didanosine (ddl) tablets, with
2. Abacavir (ABC), and
3. Efavirenz (EFV)

Didanosine must be taken alone, on an empty stomach, at least an hour before (or 2 hours after) a meal. Tablets should be dissolved in at least 30mL of water or clear apple juice. No other fruit juice may be used to dissolve tablets.

5.3 Concomitant tuberculosis

Tuberculosis is a common co-morbid illness with HIV. There are two scenarios to consider:

1. Child presents with tuberculosis before commencing antiretroviral therapy

- Complete TB therapy if possible before commencing ART OR delay ART for at least 2 months.
- If the child has failed the nevirapine vertical transmission programme or is less than 3 years old or weighs less than 10 kg, use ritonavir as the third drug.
- If the child was not on the nevirapine vertical transmission programme and is more than 3 years old and weighs more than 10 kg, use efavirenz as the third drug.
- Monitor ALT monthly.

2. Child develops tuberculosis while on antiretroviral therapy

- If the child is on lopinavir/ritonavir or nelfinavir, then switch to ritonavir.
- If the child is on nevirapine, and is less than 3 years old or weighs less than 10 kg, switch to ritonavir.
- If the child is on nevirapine and is more than 3 years old and weighs more than 10kg, switch to efavirenz.
- If the child is unable to tolerate the large number of drugs, antiretroviral therapy may have to be interrupted until TB therapy has been completed. Discuss all cases with a paediatrician with antiretroviral experience, before interrupting therapy.
- Monitor ALT monthly.

6 Adverse reactions

6.1 Grading of paediatric adverse reactions

Table 14: Grading the severity of paediatric adverse reactions (PACTG)

LABORATORY TEST ABNORMALITIES				
ITEM	GRADE 1 TOXICITY	GRADE 2 TOXICITY	GRADE 3 TOXICITY	GRADE 4 TOXICITY
Hemoglobin > 3 mo. - <2 y. o.	9.0-9.9 g/dL	7.0-8.9 g/dL	<7.0 g/dL	Cardiac failure secondary to anaemia
Hemoglobin ≥ 2 y.o.	10-10.9 g/dL	7.0-9.9 g/dL	<7.0 g/dL	Cardiac failure secondary to anaemia
Absolute Neutrophil Count	0.75-1.2 X 10 ⁹ /L	0.4-0.749 X 10 ⁹ /L	0.25-0.399X 10 ⁹ /L	<0.25 X 10 ⁹ /L
ALT (SGPT)	1.1-4.9 X upper normal limit	5.0-9.9 X upper normal limit	10.0-15.0- X upper normal limit	>15 X upper normal limit
Triglycerides	-	1.54-8.46 mmol/L	8.47-13.55 mmol/L	>13.56 mmol//L
Cholesterol	-	4.43-12.92 mmol/L	12.93-19.4 mmol/L	>19.4 mmol/L
CLINICAL ADVERSE EVENTS				
ITEM	GRADE 1 TOXICITY	GRADE 2 TOXICITY	GRADE 3 TOXICITY	GRADE 4 TOXICITY
Peripheral neuropathy	Diagnosis of peripheral neuropathy is difficult in children. Screen motor function against milestones and refer to specialist if peripheral neuropathy is suspected.			
Cutaneous / Skin Rash / Dermatitis*	-	Diffuse maculo-papular rash OR dry desquamation	Vesiculation OR ulcers	Exfoliative dermatitis OR Stevens-Johnson OR erythema multiforme OR moist desquamation

Adverse reactions will be graded according to the Paediatric AIDS Clinical Trial Group (PACTG) grading.

- Grades 1 and 2 – client remains on therapy. Repeat the test. Reassess clinically within 2 weeks.
- Grade 3 – test should be repeated in 1 week and if still Grade 3, stop ALL antiretroviral drugs and seek expert medical advice.
- Grade 4 – Stop all drugs immediately and seek specialist advice. If the patient restarts therapy after the event has resolved, and the same grade 4 event recurs, appropriate changes or withdrawal of antiretroviral therapy may need to be made. Decisions should be made on an individual basis, and discussed with experts as required.

***A rash in a child on nevirapine with mucosal involvement OR associated with fever / systemic symptoms / derangement in liver functions should be treated as a Grade 4 toxicity. All antiretrovirals should be stopped immediately. Patients at primary care should be referred to a specialist for advice regarding restarting antiretrovirals. The patient should never be rechallenged with nevirapine.**

6.2 Important adverse reactions

Table 15: Important ARV adverse reactions

Antiretroviral	Adverse Reactions
Abacavir (ABC)	<p>A potentially fatal hypersensitivity reaction develops in approximately 3-5% of patients. Symptoms usually appear within 6 weeks of treatment initiation.</p> <p>Suspect reaction if symptoms from 2 or more of the following groups are present:</p> <ul style="list-style-type: none"> • fever, • maculopapular pruritic generalised rash • gastrointestinal symptoms • other symptoms (including pharyngitis, dyspnoea, cough, musculoskeletal disorders, malaise, fatigue, lymphadenopathy and paraesthesia) <p>Never give abacavir to a child who has previously developed an abacavir hypersensitivity reaction</p>
Didanosine (ddl)	<p>Pancreatitis</p> <p>Peripheral neuropathy</p> <p>GIT effects (bloating, flatulence, nausea, diarrhoea)</p> <p>Lactic acidosis</p>
Efavirenz (EFV)	<p>CNS disturbances (dysphoria, vivid dreams, distractedness, dizziness)</p> <p>GIT symptoms</p> <p>Skin rash</p>
Lamivudine (3TC)	<p>Diarrhoea</p> <p>Pancreatitis</p> <p>Anaemia</p>
Lopinavir/Ritonavir	<p>GIT symptoms</p> <p>Lipid abnormalities</p> <p>Lipodystrophic changes</p>
Nelfinavir	<p>GIT symptoms</p> <p>Lipid abnormalities</p> <p>Lipodystrophic changes</p>
Nevirapine (NVP)	<p>Skin rash</p> <p>Nausea</p> <p>Vomiting</p> <p>Hepatitis (can be fatal)</p>
Ritonavir	<p>Bad taste</p> <p>GIT symptoms</p> <p>Raised liver enzymes</p> <p>Lipid abnormalities</p> <p>Lipodystrophic changes</p>
Stavudine (d4T)	<p>Peripheral neuropathy</p> <p>Hepatic steatosis</p> <p>Lactic acidosis</p>
Zidovudine (AZT)	<p>Bone marrow suppression (anaemia, neutropenia)</p> <p>GIT symptoms</p> <p>Myopathy</p> <p>Lactic acidosis</p>

7. Monitoring of Efficacy and Safety

Table 16 Summary: Paediatric ARV Regimens and routine monitoring during treatment

Regimen	Test	Frequency
d4T / 3TC / ritonavir	<ul style="list-style-type: none"> • CD4 • VL • Fasting cholesterol • Fasting glucose 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, 6-monthly • Baseline, 6-monthly
AZT / 3TC / ritonavir	<ul style="list-style-type: none"> • CD4 • VL • FBC • Fasting cholesterol • Fasting glucose 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, then monthly for 3 months, then 6 monthly (with CD4 and viral load) thereafter • Baseline, 6 monthly • Baseline, 6-monthly
D4T / 3TC/ lopinavir+ritonavir	<ul style="list-style-type: none"> • CD4 • VL • Fasting cholesterol • Fasting glucose 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, 6-monthly • Baseline, 6-monthly
AZT / 3TC / lopinavir+ritonavir	<ul style="list-style-type: none"> • CD4 • VL • FBC • Fasting cholesterol • Fasting glucose 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, then monthly for 3 months, then 6 monthly (with CD4 and viral load) thereafter • Baseline, 6-monthly • Baseline, 6-monthly
ddl / AZT / nevirapine	<ul style="list-style-type: none"> • CD4 • VL • FBC • ALT 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, then monthly for 3 months, then 6 monthly (with CD4 and viral load) thereafter • Baseline, week 2, 4 and 8, thereafter 6 monthly
ddl / ABC / nevirapine	<ul style="list-style-type: none"> • CD4 • VL • ALT 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, week 2, 4 and 8, thereafter 6 monthly
Ddl / AZT / EFV	<ul style="list-style-type: none"> • CD4 • VL • FBC 	<ul style="list-style-type: none"> • Staging, 6-monthly • Baseline, 6-monthly • Baseline, then monthly for 3 months, then 6 monthly (with CD4 and viral load) thereafter
Ddl / ABC / EFV	<ul style="list-style-type: none"> • CD4 • VL 	<ul style="list-style-type: none"> • Staging, 6-monthly • 6 monthly

- **Staging** = initial testing for all patients when being referred for antiretroviral therapy.
- **Baseline** = testing for ARV eligible patients, at initiation of ARVs.

Flowchart 5: First-line Treatment of Children (Schedule 1)

Please note:
Patients who have been exposed to ARVs in the past need to be discussed with an ARV expert BEFORE a treatment regimen is commenced.

< 6 months of age

> 6 months of age

IF FRIDGE AVAILABLE:
stavudine (d4T)
+
lamivudine (3TC)
+
ritonavir

IF NO FRIDGE AVAILABLE:
zidovudine (AZT)
+
lamivudine (3TC)
+
ritonavir

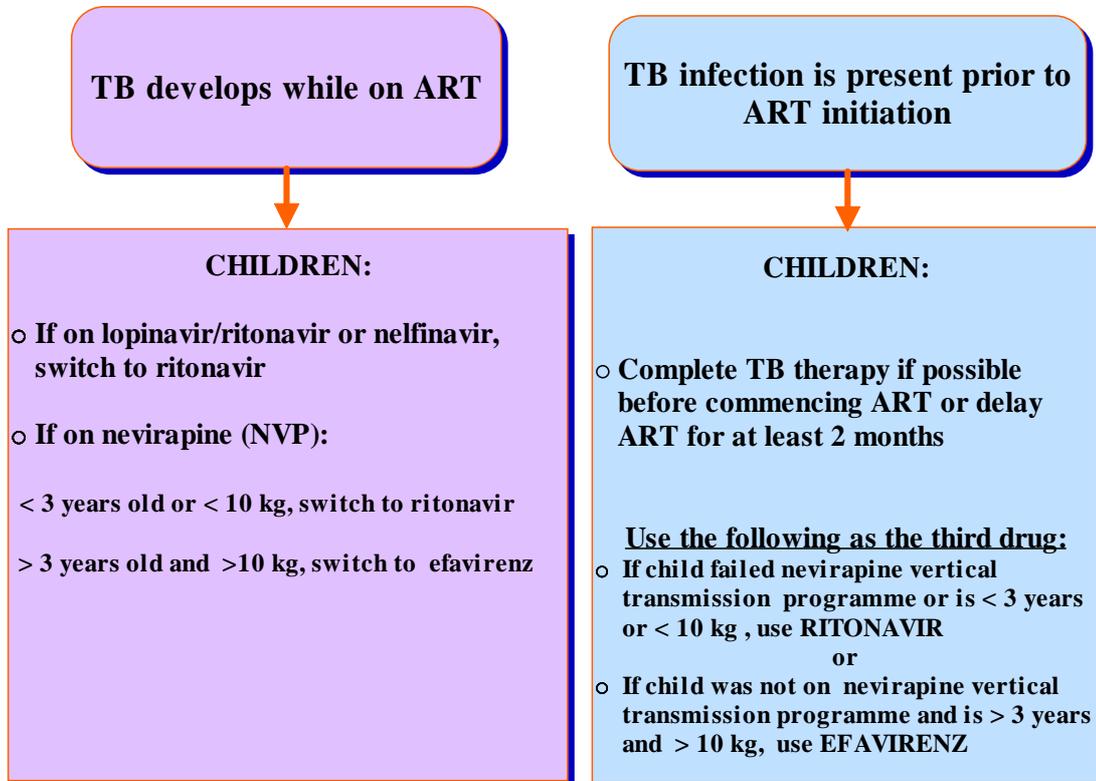
IF FRIDGE AVAILABLE:
stavudine (d4T)
+
lamivudine (3TC)
+
lopinavir/ritonavir

IF NO FRIDGE AVAILABLE:
zidovudine (AZT)
+
lamivudine (3TC)
+
lopinavir/ritonavir

Points to note:

- If ritonavir or lopinavir/ritonavir intolerance - switch to nelfinavir
- Recalculate doses according to weight or body surface at every 3 monthly visit
- Store lopinavir/ritonavir capsules and solution in refrigerator if possible, can be stored by patient for 42 days if kept below 25 ° Celsius

Flowchart 7: How to Treat Children with Concomitant Tuberculosis



Remember:

- Patients on TB medication and ARVs are taking a large number of doses of medications - do pre-emptive counselling to improve adherence
- Watch liver functions (ALT) monthly while on concomitant ARVs and TB therapy
- Recalculate doses according to weight or body surface at every 3 monthly visit

Appendix 1: Referral Letter to ARV Centre.

Please complete ALL sections of this form for your patient to be considered for therapy. Kindly call or fax to book a screening appointment.

Dear Doctor

Thank you for assessing this patient for antiretroviral therapy.

Name: _____

Address: _____

Age: _____ Contact phone 1: _____

Gender: _____ Contact phone 2: _____

He/she was diagnosed with HIV in _____ (date).

Present clinical stage: _____.

He/she has been a regular attender at this clinic since _____ (date).

He/ She has had the following WHO stage 3/4 HIV related illnesses:

	Illness:	Date:
1.		
2.		
3.		
4.		
5.		

His/her last few CD4 or total lymphocyte counts were:

List of all current medication:

	Circle one	Value:	Date:
1.	CD4 / TLC		
2.	CD4 / TLC		
3.	CD4 / TLC		
4.	CD4 / TLC		
5.	CD4 / TLC		

He/she has disclosed his/her HIV-status to at LEAST one other person, _____ (state name and relationship) who will act as a treatment supporter.

This patient is not acutely depressed. This patient has no active alcohol or other substance abuse problems.

Additional comments:

Thank you:

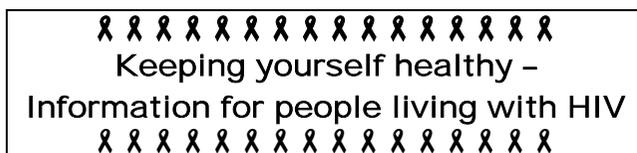
Name of health care worker: _____

Clinic name and address: _____

Clinic phone number: _____

Clinic fax number: _____

Appendix 2: HIV Info Sheet



About the Infection:

What is HIV?

HIV or the human immunodeficiency virus is the germ that causes HIV infection. Once a person becomes infected with this virus he/she is infected for life. In the long term HIV causes AIDS. AIDS may only develop after many years of being infected with HIV.

The HIV is passed from person to person in body fluids. The most likely way to catch the virus is through being exposed to an infected person's sexual fluids during sex. One in every six to eight people in South Africa is HIV positive. You do not need to have many sexual partners nor do you need to have sex often to catch HIV.

HIV may also be passed by blood or from an infected mother to her baby during pregnancy, birth or breast-feeding. It is NOT passed by kissing, sharing plates or forks, or using the same toilet.

HIV is a common illness that is already part of many households. Anyone may become infected. It is not an illness to be ashamed of and should not need to be kept a secret. If you are HIV positive you should share that knowledge with someone you trust.

The immune system:

Your body has an immune system that defends your body and keeps you well. HIV attacks and kills the "soldiers" in the immune system (called CD4 cells). Without these CD4 cells your body is unable to defend itself from other germs that are around.

It takes the HIV many years (between 3 and 20) to damage all the CD4 cells so it is a long while before there are too few to defend your body. There are many years after infection when a person can remain well.

Stages of HIV infection:

Stage 1: During this time the "soldiers" are still relatively strong. A person with stage 1 HIV usually looks and feels well. Glands causing swellings in the neck or groin are common, but these show that your immune system is fighting the HIV. If the glands become large or painful, you should let your clinic know.

Stage 2: As the CD4 count becomes lower you may notice minor illnesses, such as skin rashes or diarrhoea. You may lose some weight.

Stage 3: As the weakness progresses, you may see thrush in your mouth or catch TB. You may notice more weight loss or diarrhoea.

Stage 4: Later on you will be more at risk of picking up other illnesses, which can only happen in people with very weak immune systems (lymphocytes less than 1200). Once you have one of these illnesses, this is called AIDS. People with AIDS usually live for 1-2 years, without antiretroviral therapy.

Some of these illnesses, particularly when diagnosed early, are treatable. Some others can be prevented. Go and see your doctor as soon as you are worried.

It is impossible to tell from the examination or blood results when a person was infected with the virus. HIV infection progresses at different speeds in different people.

Living with HIV

One of the most important things to remember is that you have an illness that you have to LIVE with. You may well get sick in time, but there are many things that can be done to remain well for years.

If possible, choose a close friend or relative, someone you can trust, to tell about your HIV status. Keeping it a secret is a big burden to carry. Having someone to talk to helps a great deal. There are a number of support groups and counselling agencies where you can meet others living with HIV and discuss common issues, for example:

- Sizophila (Gugulethu) 638-6488
- Red Cross Society (Wynberg) 797-5360
- ATICC (Cape Town) 797-3327
- Life-line Cape Town 461-1111, Gugulethu 637-3009, Khayelitsha 361-5855
- Wola Nani (Khayelitsha) 361-1116

Staff at your clinic will also be willing to help where they can.

General health:

Make sure you eat healthily, get enough exercise and sleep well. Eating healthily need not be expensive. Here are a few tips:

- Use whole wheat or brown bread instead of white.
- Use beans, lentils and pea products often. If you don't have money to buy meat these can be used instead.
- Use fish, chicken and eggs when you can.
- Buy fresh vegetables and fruit in season. Use more vegetables if fruit is expensive. Try not to overcook the vegetables.
- Grow your own vegetables if possible.
- Cook potatoes and sweet potatoes with the skins on.

Preventing infections: Try not to get into close contact with people who have a cold or a chest infection or people with TB. Do not allow people to smoke in your house. Make sure you wash your hands with soap before preparing food and wash all fresh food well before cooking. Try not to eat raw foods, especially meat and chicken. Cook eggs till the yolk is hard.

Symptoms to worry about:

If you notice any of these things, please visit your clinic for a check-up:

- Ongoing cough (>2 weeks),
- Marked loss of weight (a few kilograms)
- Ongoing night sweating (> 2 weeks)
- Loose stools or diarrhoea for more than 2 weeks
- Skin rashes that bother you
- Severe headaches or depression

- Any other symptoms that worry you or are worse than you would expect in a person without HIV.

It is really important that your doctor or nurse knows about you being HIV positive. You may need treatment which is different from a person without HIV.

Preventing the spread of HIV:

Between adults: The most common means of spreading HIV in South Africa is from man to woman or woman to man during sexual intercourse. HIV is carried in the sexual fluids.

To reduce the chance of coming into contact with another person's sexual fluids a condom (male or female) should be used every time you have sex. Condoms are available free from most day hospitals, counselling services and family planning clinics.

From mother to child: If a pregnant mother knows she has HIV she should ask her doctor or nurse where she can access the pMTCT (prevention of mother to child transmission) programme. Antiretrovirals may be given in the last few weeks of pregnancy and/or in labour. These drugs push the levels of HIV down in the blood and reduce the risk of the baby becoming HIV positive.

Another way of reducing this risk is to bottle-feed the baby (breast-milk feeds may cause the baby to become infected). As formula feed can be expensive, HIV-positive mothers will be supplied with it free for the first 6 months of

their baby's life. If a baby is not fed enough milk he/she can become ill from malnutrition.

If a baby is known to be HIV positive already, breast-feeding should be continued.

Why does my child get ill when I am still well?

HIV often progresses more rapidly in a child. You can think of it as their immune system or "soldier cells" also being young and less able to fight off the HIV, which is the same virus that would infect an adult.

What of the future?

As time passes people with HIV are able to stay well for longer and longer. This is because we have learnt about the virus and about preventing and treating the opportunistic infections. Living healthily also may delay the onset of illness. More treatments are becoming available that may further delay the onset of AIDS.

Prepared by Dr. Catherine Orrell <catherine.orrell@hiv-research.org.za> 



Pregnancy:

We do not know everything that these medicines might do to an unborn baby. You will be asked to use condoms EVERY TIME YOU HAVE SEX, for the whole time you are on the study. The injection or pill is NOT enough, as some of the anti-HIV drugs may lessen their effect. We will ask you to use both condoms and the pill or injection.

If you fall pregnant there is a chance the baby may be born with abnormalities, although you will be changed to the safest medication possible.

What should I be taking?

There are three groups of antiretroviral (anti-HIV) medicines available. These include medicines such as:

1. AZT, 3TC d4T and ddI – NRTIs or nucs (backbone therapy)
2. nevirapine, efavirenz – NNRTIs or non-nucs.
3. lopinavir, saquinavir, ritonavir - protease inhibitors

One medicine is not enough. The HIV learns about it and grows through it after only a few months (i.e. becomes resistant). You need to make sure you are taking at LEAST 3 medicines from the above groups.

How do I take them?

The medicines are taken by mouth, usually 1 or 2 times a day, that is, every 12 or 24 hours. There may be large numbers of tablets (sometimes 7 or more a day). Before beginning treatment you must know that these medicines **HAVE TO BE TAKEN, as directed, EVERY SINGLE DAY**. This is very important.

If you miss doses the HIV can become resistant to the medicines and they will no longer work to suppress your virus. Missing just one dose every two weeks can quickly cause the virus to become resistant.

If you think you cannot take them every day, you should not start these medicines. Once the virus is resistant, it is VERY DIFFICULT to treat it and you may have to stop the treatment as it is not working. You really only have **one good chance** to make the medicines work for you.

Your clinic team has been trained to support you in taking your treatment. If you have any problems with taking your tablets, it is VERY important that you let the nurse or doctor know. They can help you with advice about diaries or using a pillbox to remind you about your medicines.

You can also join a support group with other people on antiretroviral therapy to discuss the best way to manage these tablets.

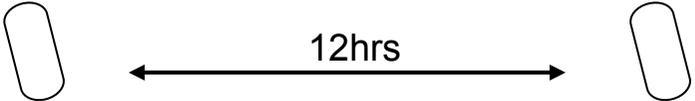
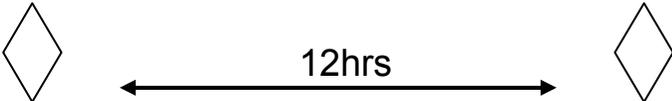
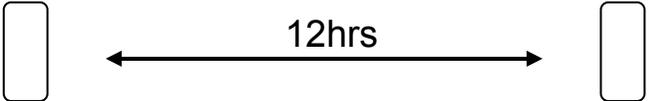
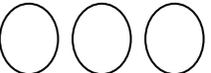
How long do I take antiretrovirals for?

Once you begin treatment you will be taking it for as long as it continues to work against your virus. If you take the medications as prescribed, this could be many many years. You should think of it as a life-long commitment to the treatment programme.

Compiled by Dr Catherine Orrell
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Appendix 4 - Treatment Chart for schedule 1 (Adults)

Medicine	Timing of doses	Possible side effects
<p>1. d4T</p>	<p>morning e.g. 7am</p> <p>12hrs</p> <p>night e.g. 7pm</p> 	<p>Numbness or pain in the feet, abdominal pain, hepatitis</p>
<p>2. 3TC</p>		<p>Diarrhoea, headache</p>
<p>3. nevirapine</p>		<p>Skin rash (allergy), hepatitis</p>
<p>OR</p> <p>3. efavirenz</p>	<p>24hrs</p> <p>Only taken once a day, at night night.</p> 	<p>Skin rash (allergy), vivid dreams, dizziness, sleep changes in first 4 weeks</p>
<p>Note to health care worker: Please cross out either nevirapine or efavirenz, depending on regimen</p>		<p>Most side effects get better after 1 to 2 months of treatment</p>

Appendix 5: Paediatric Dosing Schedule

How to determine body surface area (BSA):

Method 1:

The body surface area of a child can be determined using the nomogram for infants and young children as stated in the Handbook of Paediatrics, 5th edition or on page 297 of the Paediatric Standard Treatment Guidelines 1998 (purple book)

Method 2:

Use the following formula:

$$\text{BSA} = \sqrt{\frac{\text{Height (cm)} \times \text{weight (Kg)}}{3600}}$$

For example:

Height: 80 cm

Weight: 12 kg

$$\text{BSA} = \sqrt{\frac{80 \text{ (cm)} \times 12 \text{ (Kg)}}{3600}}$$

Use your calculator in the following way:

Step 1: Press: 80 x 12 and =

Step 2: Press: ÷ 3600 and =

Step 3: Press: square root button

Your answer = 0.52 m²

Antiretroviral	Dosage	Important notes																																																						
Zidovudine (AZT) Retrovir®	Neonatal/Infant dose (infants aged < 90 days): Oral: 2mg per kg of body weight every six hours. (Need to reduce dose for premature infants) ¹	Available as: Syrup: 10mg/ml Capsules: 100 mg & 250 mg Tablets: 300 mg																																																						
	Volume of Zidovudine (AZT) 10 mg/ml for children between 3 months and 12 years: ³	Do not exceed the adult dose of 300mg every 12 hours																																																						
	<table border="1"> <thead> <tr> <th data-bbox="510 550 786 608">Body surface (m²)</th> <th data-bbox="786 550 1173 608">Volume (ml) of MORNING dose</th> <th data-bbox="1173 550 1576 608">Volume (ml) of NIGHT dose (12 hours after morning dose)</th> </tr> </thead> <tbody> <tr><td>0.30</td><td>5.5</td><td>5.5</td></tr> <tr><td>0.35</td><td>6.0</td><td>6.0</td></tr> <tr><td>0.40</td><td>7.0</td><td>7.0</td></tr> <tr><td>0.45</td><td>8.0</td><td>8.0</td></tr> <tr><td>0.50</td><td>9.0</td><td>9.0</td></tr> <tr><td>0.55</td><td>10.0**</td><td>10.0**</td></tr> <tr><td>0.60</td><td>11.0</td><td>11.0</td></tr> <tr><td>0.65</td><td>12.0</td><td>12.0</td></tr> <tr><td>0.70</td><td>13.0</td><td>13.0</td></tr> <tr><td>0.75</td><td>13.5</td><td>13.5</td></tr> <tr><td>0.80</td><td>14.5</td><td>14.5</td></tr> <tr><td>0.85</td><td>15.0*</td><td>15.0*</td></tr> <tr><td>0.90</td><td>16.0</td><td>16.0</td></tr> <tr><td>0.95</td><td>17.0</td><td>17.0</td></tr> <tr><td>1.00</td><td>18.0</td><td>18.0</td></tr> <tr><td>1.05</td><td>19.0</td><td>19.0</td></tr> <tr><td>1.10</td><td>20.0**</td><td>20.0**</td></tr> </tbody> </table>	Body surface (m ²)	Volume (ml) of MORNING dose	Volume (ml) of NIGHT dose (12 hours after morning dose)	0.30	5.5	5.5	0.35	6.0	6.0	0.40	7.0	7.0	0.45	8.0	8.0	0.50	9.0	9.0	0.55	10.0**	10.0**	0.60	11.0	11.0	0.65	12.0	12.0	0.70	13.0	13.0	0.75	13.5	13.5	0.80	14.5	14.5	0.85	15.0*	15.0*	0.90	16.0	16.0	0.95	17.0	17.0	1.00	18.0	18.0	1.05	19.0	19.0	1.10	20.0**	20.0**	** These doses can be administered as 100mg capsules (=10ml of suspension)
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The therapeutic dose of zidovudine is 180 mg/m² every 12 hours with a maximum dose of 200 mg every 12 hours. ^{1,2}	* This dose can be administered as half a 300mg tablet																																																							
	Storage: Store all preparations below 30 °C ⁴																																																							

Antiretroviral	Dosage	Important notes																																																																					
<p data-bbox="226 762 490 868">Lamivudine (3TC) 3TC®</p>	<p data-bbox="512 292 1547 360">Volume of Lamivudine (3TC) 10 mg/ml oral solution for children between 3 months and 12 years: ³</p>	<p data-bbox="1659 292 1951 395">Available as: 150 mg tablets 10mg/ml oral solution</p> <p data-bbox="1659 440 2074 509">Do not exceed the adult dose of 150mg every 12 hours</p> <p data-bbox="1659 549 2107 579">Can be taken with or without food</p> <p data-bbox="1659 624 2085 692">Dosage adjustments are required in renal failure</p> <p data-bbox="1659 1067 2107 1171">Storage: Tablets: Store at or below 30 °C Solution: Store at or below 25 °C ⁵</p>																																																																					
	<table border="1" data-bbox="517 395 1581 1169"> <thead> <tr> <th data-bbox="517 395 790 459">Weight (kg)</th> <th data-bbox="790 395 1171 459">Volume (ml) of MORNING dose</th> <th data-bbox="1171 395 1581 459">Volume (ml) of NIGHT dose (12 hours after morning dose)</th> </tr> </thead> <tbody> <tr><td>4</td><td>1.5</td><td>1.5</td></tr> <tr><td>5</td><td>2.0</td><td>2.0</td></tr> <tr><td>6</td><td>2.5</td><td>2.5</td></tr> <tr><td>7</td><td>3.0</td><td>3.0</td></tr> <tr><td>8</td><td>3.0</td><td>3.0</td></tr> <tr><td>9</td><td>3.5</td><td>3.5</td></tr> <tr><td>10</td><td>4.0</td><td>4.0</td></tr> <tr><td>11</td><td>4.5</td><td>4.5</td></tr> <tr><td>12</td><td>5.0</td><td>5.0</td></tr> <tr><td>13</td><td>5.0</td><td>5.0</td></tr> <tr><td>14</td><td>5.5</td><td>5.5</td></tr> <tr><td>15</td><td>6.0</td><td>6.0</td></tr> <tr><td>16</td><td>6.5</td><td>6.5</td></tr> <tr><td>17</td><td>7.0</td><td>7.0</td></tr> <tr><td>18</td><td>7.0</td><td>7.0</td></tr> <tr><td>19</td><td>7.5</td><td>7.5</td></tr> <tr><td>20</td><td>8.0</td><td>8.0</td></tr> <tr><td>21</td><td>8.5</td><td>8.5</td></tr> <tr><td>22</td><td>9.0</td><td>9.0</td></tr> <tr><td>23</td><td>9.0</td><td>9.0</td></tr> <tr><td>24</td><td>9.5</td><td>9.5</td></tr> <tr><td>25</td><td>10.0</td><td>10.0</td></tr> </tbody> </table> <p data-bbox="512 1209 1619 1278">The therapeutic dosage of lamivudine is 4 mg per kg of body weight twice a day up to a maximum of 300 mg daily ¹</p>		Weight (kg)	Volume (ml) of MORNING dose	Volume (ml) of NIGHT dose (12 hours after morning dose)	4	1.5	1.5	5	2.0	2.0	6	2.5	2.5	7	3.0	3.0	8	3.0	3.0	9	3.5	3.5	10	4.0	4.0	11	4.5	4.5	12	5.0	5.0	13	5.0	5.0	14	5.5	5.5	15	6.0	6.0	16	6.5	6.5	17	7.0	7.0	18	7.0	7.0	19	7.5	7.5	20	8.0	8.0	21	8.5	8.5	22	9.0	9.0	23	9.0	9.0	24	9.5	9.5	25	10.0	10.0
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Antiretroviral	Dosage	Important notes										
<p>Didanosine (ddI)</p> <p>Videx®</p>	<p>Dosage: Neonatal/Infant dose (infants aged < 90 days): 50 mg per m² of body surface area every 12 hours. Paediatric usual dose: 120 mg per m² of body surface area every 12 hours. Paediatric dosage range: 90 to 150 per m² of body surface area every 12 hours. ¹</p> <p><i>Dosing guidelines:</i> ⁶</p>	<p>Available as 25, 50, 100 and 150 mg tablets, store at room temperature</p> <p>Food decreases absorption; administer on an empty stomach (30 minutes before or two hours after a meal)</p> <p><i>How to give tablets:</i></p> <ol style="list-style-type: none"> The tablets should be chewed, or thoroughly dispersed in: 30 ml water for 2-4 tablets 15 ml water for 1 tablet. An equal amount of clear apple juice may be added to the above dispersion. Stir just prior to consumption. Dispersion with apple juice is stable at < 25 °C for up to one hour. ⁶ <p>Storage: Store at room temperature (not exceeding 25°C)</p>										
	<table border="1"> <thead> <tr> <th data-bbox="510 550 1088 587">Body Surface Area (m²)</th> <th data-bbox="1088 550 1639 587">Amount of Videx tablets</th> </tr> </thead> <tbody> <tr> <td data-bbox="510 587 1088 659">1.1 – 1.4</td> <td data-bbox="1088 587 1639 659">100 mg every 12 hours (give as 2 x 50 mg tablets per dose)</td> </tr> <tr> <td data-bbox="510 659 1088 730">0.8 – 1.0</td> <td data-bbox="1088 659 1639 730">75 mg every 12 hours (give as 1 x 25 mg plus 1 x 50 mg tablet per dose)</td> </tr> <tr> <td data-bbox="510 730 1088 802">0.5 – 0.7</td> <td data-bbox="1088 730 1639 802">50 mg every 12 hours (give as 2 x 25 mg tablets per dose)</td> </tr> <tr> <td data-bbox="510 802 1088 882">≤ 0.4</td> <td data-bbox="1088 802 1639 882">25 mg every 12 hours (give as 1 x 25mg tablet per dose)</td> </tr> </tbody> </table>		Body Surface Area (m ²)	Amount of Videx tablets	1.1 – 1.4	100 mg every 12 hours (give as 2 x 50 mg tablets per dose)	0.8 – 1.0	75 mg every 12 hours (give as 1 x 25 mg plus 1 x 50 mg tablet per dose)	0.5 – 0.7	50 mg every 12 hours (give as 2 x 25 mg tablets per dose)	≤ 0.4	25 mg every 12 hours (give as 1 x 25mg tablet per dose)
	Body Surface Area (m ²)		Amount of Videx tablets									
	1.1 – 1.4		100 mg every 12 hours (give as 2 x 50 mg tablets per dose)									
	0.8 – 1.0		75 mg every 12 hours (give as 1 x 25 mg plus 1 x 50 mg tablet per dose)									
	0.5 – 0.7		50 mg every 12 hours (give as 2 x 25 mg tablets per dose)									
≤ 0.4	25 mg every 12 hours (give as 1 x 25mg tablet per dose)											
<p>To ensure a sufficient amount of antacid is received, each dose must be given as: 2 tablets for children > 1 year 1 tablet for children < 1 year E.g. For a 100 mg dose in a child > 1 year two 50mg tablets may be used. To prevent overdose of the antacid or phenylalanine component of the tablets no more than 4 tablets should be taken at each dose.</p>												

Antiretroviral	Dosage			Important notes
<p data-bbox="226 759 450 791">Abacavir (ABC)</p> <p data-bbox="226 834 349 866">Ziagen®</p>	Volume of Abacavir (ABC) oral solution (20 mg/ml) for children between 3 months and 12 years:			<p data-bbox="1662 296 1906 395">Available as: Tablets: 300mg Solution: 20mg/ml</p> <p data-bbox="1662 440 2078 507">Do not exceed adult dose of 300 mg every 12 hours ¹</p> <p data-bbox="1662 552 2063 619">Can be given without regard to food</p> <p data-bbox="1662 663 2101 730">Not approved for infants less than three months of age</p> <p data-bbox="1662 1110 1962 1177">Storage: Store at or below 30 °C</p> <p data-bbox="1662 1222 2092 1289">Discard oral solution two months after first opening ⁸</p>
	Weight (kg)	Volume (ml) of MORNING dose	Volume (ml) of NIGHT dose (12 hours after morning dose)	
	4	1.6	1.6	
	5	2	2	
	6	2.4	2.4	
	7	2.8	2.8	
	8	3.2	3.2	
	9	3.6	3.6	
	10	4	4	
	11	4.4	4.4	
	12	4.8	4.8	
	13	5.2	5.2	
	14	5.6	5.6	
	15	6	6	
	16	6.4	6.4	
	17	6.8	6.8	
	18	7.2	7.2	
	19	7.6	7.6	
	20	8	8	
	21	8.4	8.4	
	22	8.8	8.8	
	23	9.2	9.2	
	24	9.6	9.6	
	25	10	10	
	26	10.4	10.4	
	27	10.8	10.8	
	28	11.2	11.2	
	29	11.6	11.6	
	30	12	12	
	31	12.4	12.4	
32	12.8	12.8		
33	13.2	13.2		
34	13.6	13.6		
35	14	14		
36	14.4	14.4		
37	14.8	14.8		
>37	300 mg tablet	300 mg tablet		
The paediatric / adolescent dose: 8 mg/kg of body weight twice daily ¹				

Antiretroviral	Dosage				Important notes	
<p data-bbox="226 754 479 786">Nevirapine (NVP)</p> <p data-bbox="226 831 389 863">Viramune®</p>	Volume of Nevirapine 10 mg/ml for children between 2 months and 8 years: ³				<p data-bbox="1664 298 1944 395">Available as: Suspension: 10mg/ml Tablets: 200mg</p> <p data-bbox="1664 440 2101 507">Do not exceed the maximum dose of 200mg (20ml) every 12 hours</p> <p data-bbox="1664 959 2096 1056">Storage: Tablets supplied in plastic bottles must be stored below 25 °C</p> <p data-bbox="1664 1107 2107 1204">Tablets in blister packs and the oral solution must be stored below 30 °C.</p> <p data-bbox="1664 1249 2029 1281">Do not refrigerate solution. ⁹</p>	
	Weight (kg)	Volume (ml) for the first 14 days ONCE daily	Volume (ml) of MORNING dose after 14 days	Volume (ml) of NIGHT dose after 14 days (12 hours after morning dose)		
	4	1.5	3.0	3.0		
	5	2.0	3.5	3.5		
	6	2.5	4.0	4.0		
	7	3.0	5.0	5.0		
	8	3.0	5.5	5.5		
	9	3.5	6.0	6.0		
	10	4.0	7.0	7.0		
	11	4.5	8.0	8.0		
	12	5.0	8.5	8.5		
	13	5.0	9.0	9.0		
	14	5.5	10.0	10.0		
	15	6.0	10.5	10.5		
	16	6.5	11.0	11.0		
	17	7.0	12.0	12.0		
	18	7.0	12.5	12.5		
	19	7.5	13.5	13.5		
	20	8.0	14.0	14.0		
	21	8.5	15.0	15.0		
	22	9.0	15.5	15.5		
	23	9.0	16.0	16.0		
	24	9.5	17.0	17.0		
	25	10.0	17.5	17.5		
	<p data-bbox="510 1161 1644 1259"><i>The recommended dose of nevirapine suspension for babies and children 2 months up to 8 years of age is an initial dose (lead-in period) of 4 mg/kg ONCE daily for 14 days followed by 7 mg/kg twice a day.</i></p> <p data-bbox="510 1265 1644 1315">For children > 8 years: 4mg/kg ONCE daily for two weeks followed by 4mg/kg twice daily thereafter. ⁹</p>					

Antiretroviral	Dosage		Important notes
<p>Efavirenz (EFV)</p> <p>Stocrin®</p>	Recommended doses for efavirenz: ¹		<p>Available as: Capsules: 50mg & 200mg</p> <p>Do not exceed the adult dose of 600mg once daily</p> <p>May be taken with or without food, avoid high fat meals.</p> <p>Capsules may be opened and added to liquids or foods, but EFV has a peppery taste. ¹</p> <p>No data available on the appropriate dosage for children under three years old</p> <p>Storage: Store capsules at room temperature below 30 °C ¹⁰</p>
	Body weight (kg)	Dose administered once daily (Preferably at bedtime)	
	10 to <15 kg	200mg	
	15 to <20 kg	250 mg	
	20 to <25 kg	300 mg	
	25 to <32.5 kg	350 mg	
	32.5 to <40 kg	400 mg	
	≥40 kg	600 mg	

Antiretroviral	Dosage	Important notes																																																																								
<p data-bbox="226 762 371 791">Nelfinavir</p> <p data-bbox="226 834 383 863">Vira-cept®</p>	<p data-bbox="512 328 1615 464"><i>The recommended oral dose for patients 2 to 13 years of age is 25 to 30 mg/kg per dose, three times daily with a meal or light snack. The dose to be administered three times daily, using a combination of both the 1 gram and 5 gram scoop, is described below:</i>¹¹</p>	<p data-bbox="1659 292 1928 387">Available as: Tablets: 250 mg Oral Powder: 50 mg/g</p> <p data-bbox="1659 427 2107 523">Do not exceed the adult dose of 1250 mg every 12 hours or 750 mg every 8 hours (tds)</p> <p data-bbox="1659 563 1917 592">Administer with food</p> <p data-bbox="1659 632 2119 887">Advise the patient to use the handle of the second scoop to scrape off extra powder and obtain a level scoop Powder may be mixed with a small amount of water, milk, formula, soy formula, soy milk, dietary supplements,¹¹ pudding or ice cream¹</p> <p data-bbox="1659 903 2107 967">Once mixed, the entire contents must be consumed.¹¹</p> <p data-bbox="1659 975 2096 1134">Tablets readily dissolve in water and produce a dispersion that can be mixed with milk or chocolate milk; tablets can also be crushed and administered with pudding¹</p> <p data-bbox="1659 1278 1872 1334">Storage: Store below 25 °C</p>																																																																								
	<table border="1" data-bbox="517 472 1637 967"> <thead> <tr> <th data-bbox="517 472 719 655">Body weight (kg)</th> <th data-bbox="719 472 864 655">Total grams of powder</th> <th data-bbox="864 472 1032 655">Number of level 5ml medicine measures</th> <th data-bbox="1032 472 1155 655">White Scoop (1 gram)</th> <th data-bbox="1155 472 1245 655"></th> <th data-bbox="1245 472 1413 655">Blue scoop (5 grams)</th> <th data-bbox="1413 472 1514 655"></th> <th data-bbox="1514 472 1637 655">Number of tablets</th> </tr> </thead> <tbody> <tr> <td data-bbox="517 655 719 695">7 to < 8.5</td> <td data-bbox="719 655 864 695">4</td> <td data-bbox="864 655 1032 695">1</td> <td data-bbox="1032 655 1155 695">4</td> <td data-bbox="1155 655 1245 695">plus</td> <td data-bbox="1245 655 1413 695">0</td> <td data-bbox="1413 655 1514 695"></td> <td data-bbox="1514 655 1637 695">-</td> </tr> <tr> <td data-bbox="517 695 719 735">8.5 to < 10.5</td> <td data-bbox="719 695 864 735">5</td> <td data-bbox="864 695 1032 735">1 ¼</td> <td data-bbox="1032 695 1155 735">0</td> <td data-bbox="1155 695 1245 735">plus</td> <td data-bbox="1245 695 1413 735">1</td> <td data-bbox="1413 695 1514 735"></td> <td data-bbox="1514 695 1637 735">-</td> </tr> <tr> <td data-bbox="517 735 719 775">10.5 to <12</td> <td data-bbox="719 735 864 775">6</td> <td data-bbox="864 735 1032 775">1 ½</td> <td data-bbox="1032 735 1155 775">1</td> <td data-bbox="1155 735 1245 775">plus</td> <td data-bbox="1245 735 1413 775">1</td> <td data-bbox="1413 735 1514 775"></td> <td data-bbox="1514 735 1637 775">-</td> </tr> <tr> <td data-bbox="517 775 719 815">12 < 14</td> <td data-bbox="719 775 864 815">7</td> <td data-bbox="864 775 1032 815">1 ¾</td> <td data-bbox="1032 775 1155 815">2</td> <td data-bbox="1155 775 1245 815">plus</td> <td data-bbox="1245 775 1413 815">1</td> <td data-bbox="1413 775 1514 815"></td> <td data-bbox="1514 775 1637 815">-</td> </tr> <tr> <td data-bbox="517 815 719 855">14 to < 16</td> <td data-bbox="719 815 864 855">8</td> <td data-bbox="864 815 1032 855">2</td> <td data-bbox="1032 815 1155 855">3</td> <td data-bbox="1155 815 1245 855">plus</td> <td data-bbox="1245 815 1413 855">1</td> <td data-bbox="1413 815 1514 855"></td> <td data-bbox="1514 815 1637 855">-</td> </tr> <tr> <td data-bbox="517 855 719 895">16 to < 18</td> <td data-bbox="719 855 864 895">9</td> <td data-bbox="864 855 1032 895">2 ¼</td> <td data-bbox="1032 855 1155 895">4</td> <td data-bbox="1155 855 1245 895">plus</td> <td data-bbox="1245 855 1413 895">1</td> <td data-bbox="1413 855 1514 895"></td> <td data-bbox="1514 855 1637 895">-</td> </tr> <tr> <td data-bbox="517 895 719 935">18 to < 23</td> <td data-bbox="719 895 864 935">10</td> <td data-bbox="864 895 1032 935">2 ½</td> <td data-bbox="1032 895 1155 935">0</td> <td data-bbox="1155 895 1245 935">plus</td> <td data-bbox="1245 895 1413 935">2</td> <td data-bbox="1413 895 1514 935">Or</td> <td data-bbox="1514 895 1637 935">2</td> </tr> <tr> <td data-bbox="517 935 719 967">≥ 23</td> <td data-bbox="719 935 864 967">15</td> <td data-bbox="864 935 1032 967">3 ¾</td> <td data-bbox="1032 935 1155 967">0</td> <td data-bbox="1155 935 1245 967">plus</td> <td data-bbox="1245 935 1413 967">3</td> <td data-bbox="1413 935 1514 967">Or</td> <td data-bbox="1514 935 1637 967">3</td> </tr> </tbody> </table>	Body weight (kg)	Total grams of powder	Number of level 5ml medicine measures	White Scoop (1 gram)		Blue scoop (5 grams)		Number of tablets	7 to < 8.5	4	1	4	plus	0		-	8.5 to < 10.5	5	1 ¼	0	plus	1		-	10.5 to <12	6	1 ½	1	plus	1		-	12 < 14	7	1 ¾	2	plus	1		-	14 to < 16	8	2	3	plus	1		-	16 to < 18	9	2 ¼	4	plus	1		-	18 to < 23	10	2 ½	0	plus	2	Or	2	≥ 23	15	3 ¾	0	plus	3	Or	3	
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<p>Ritonavir</p> <p>Norvir®</p>	<p>Important: To minimise nausea/vomiting start at 250mg/m² every 12 hours and increase to 400mg/m² every 12 hours over 5 days ^{1,3}</p> <p>Volume of ritonavir at 400mg/m² (solution provides 80mg/ml): ³</p> <table border="1" data-bbox="517 507 1608 1118"> <thead> <tr> <th>Body surface (m²)</th> <th>Volume (ml) of MORNING dose</th> <th>Volume (ml) of NIGHT dose (12 hours after morning dose)</th> </tr> </thead> <tbody> <tr><td>0.30</td><td>1.5</td><td>1.5</td></tr> <tr><td>0.35</td><td>1.75</td><td>1.75</td></tr> <tr><td>0.40</td><td>2.0</td><td>2.0</td></tr> <tr><td>0.45</td><td>2.25</td><td>2.25</td></tr> <tr><td>0.50</td><td>2.5**</td><td>2.5**</td></tr> <tr><td>0.55</td><td>2.75</td><td>2.75</td></tr> <tr><td>0.60</td><td>3.0</td><td>3.0</td></tr> <tr><td>0.65</td><td>3.25</td><td>3.25</td></tr> <tr><td>0.70</td><td>3.5</td><td>3.5</td></tr> <tr><td>0.75</td><td>3.75</td><td>3.75</td></tr> <tr><td>0.80</td><td>4.0</td><td>4.0</td></tr> <tr><td>0.85</td><td>4.25</td><td>4.25</td></tr> <tr><td>0.90</td><td>4.5</td><td>4.5</td></tr> <tr><td>0.95</td><td>4.75</td><td>4.75</td></tr> <tr><td>1.00</td><td>5.0**</td><td>5.0**</td></tr> <tr><td>1.05</td><td>5.25</td><td>5.25</td></tr> <tr><td>1.10</td><td>5.5</td><td>5.5</td></tr> </tbody> </table>	Body surface (m ²)	Volume (ml) of MORNING dose	Volume (ml) of NIGHT dose (12 hours after morning dose)	0.30	1.5	1.5	0.35	1.75	1.75	0.40	2.0	2.0	0.45	2.25	2.25	0.50	2.5**	2.5**	0.55	2.75	2.75	0.60	3.0	3.0	0.65	3.25	3.25	0.70	3.5	3.5	0.75	3.75	3.75	0.80	4.0	4.0	0.85	4.25	4.25	0.90	4.5	4.5	0.95	4.75	4.75	1.00	5.0**	5.0**	1.05	5.25	5.25	1.10	5.5	5.5	<p>Available as: Capsules: 100 mg Oral solution: 80mg/ml</p> <p>Do not exceed the adult dose of 600mg every 12 hours (equal to 7.5ml every 12 hours)</p> <p>Administer with food</p> <p>** These doses can be given as 100mg capsules (equal to 1.25ml of solution)</p> <p>If prescribed with didanosine, there should be two hours between taking each of the drugs ¹</p> <p>Storage: Capsules: In refrigerator until dispensed. Refrigeration not required if used within 30 days and stored below 25 °C Solution: Store at room temperature, (20 – 25 °C). Do not refrigerate ¹²</p>
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Antiretroviral	Dosage	Important notes	
Lopinavir/ Ritonavir Kaletra®	Volume of Kaletra solution (1ml contains 80 mg lopinavir and 20 mg ritonavir) administered every 12 hours in children 6 months to 12 years of age: ¹³	Available as: Solution: 80mg lopinavir & 20mg ritonavir per ml Capsules: 133.3mg lopinavir & 33.3mg ritonavir Do not exceed the adult dose of 5.0 ml or three capsules every 12 hours Take with food Use adult dose for children greater than 12 years of age Storage: Store in refrigerator if possible. Can be stored by patient for 42 days (CDC says 2 months) if kept below 25 ° Celsius. ¹³	
	Weight (kg)		Volume of oral solution
	7-10kg		1.25 ml twice daily
	>10-<15kg		1.75 ml twice daily
	15-20kg		2.25 ml twice daily
	>20-25kg		2.75 ml twice daily
	>25-30kg		3.50 ml twice daily
	>30-35kg		4.00 ml twice daily
	>35- 40kg		4.75 ml twice daily
	>40kg		5.0 ml twice daily or 3 capsules twice daily
<i>The recommended dose for children between 6 months to 12 years of age is: 7 kg to <15 kg: 12/3 mg/kg of Kaletra solution twice daily 15 to 40 kg: 10/2.5 mg/kg of Kaletra solution twice daily</i> ¹³			

References:

1. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection, September 22, 2003. The Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children (<http://AIDSinfo.nih.gov>)
2. South African Medicines Formulary. 6th ed
3. Personal communication, Prof Paul Roux
4. Retrovir Package Insert
5. 3TC Package Insert
6. Videx Package Insert
7. Zerit Package Insert
8. Ziagen Package Insert
9. Viramune Package Insert
10. Stocrin Package Insert
11. Vira-Cept Package Insert
12. Norvir Package Insert
13. Kaletra Package Insert