

STEP-BY-STEP GUIDE
FOR THE
MANAGEMENT OF CHILDREN ON ART

4th Edition

Compiled by:

NH McKerrow, CR Stephen, SE Purchase, R Reddy
Department of Paediatrics
Pietermaritzburg Metropolitan Hospitals Complex, KwaZulu-Natal

KL Naidoo
Department of Paediatrics
King Edward VIII Hospital
Durban, KwaZulu-Natal

M Archary
Paediatric Infectious Diseases Unit
University of KwaZulu-Natal, Durban

J Houghton
CHIVA, South Africa

August 2010
Pietermaritzburg

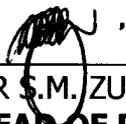
ISBN No: 978-0-620-47492-4

Foreword

HIV/AIDS continues to play a significant role in the morbidity and mortality of children in southern Africa. In South Africa it is an underlying factor in 56.5% of hospital deaths amongst children below 5 years of age. In light of this the revised National PMTCT and ART protocols introduced on 1 April 2010 are welcomed. The challenge facing this province is to convert sound policy into effective practice and to ensure easy access for all our children to appropriate preventive and treatment programmes.

A number of tools are available within our health service to assist clinicians at all levels of care with this process of implementation. These include an IMCI HIV/AIDS algorithm for use at the primary health care level and this Step-by-Step guide for use at all levels of care.

The fourth edition of this handbook is an accessible guide to assist health care workers in providing antiretroviral therapy to HIV infected children. It includes the latest policies, protocols and practices in an easy to use and practical format that will aid both experienced and inexperienced clinicians. All clinicians working with children in this province are encouraged to use this handbook so that we are able to ensure that our children receive appropriate care of an acceptable standard.



DR S.M. ZUNGU

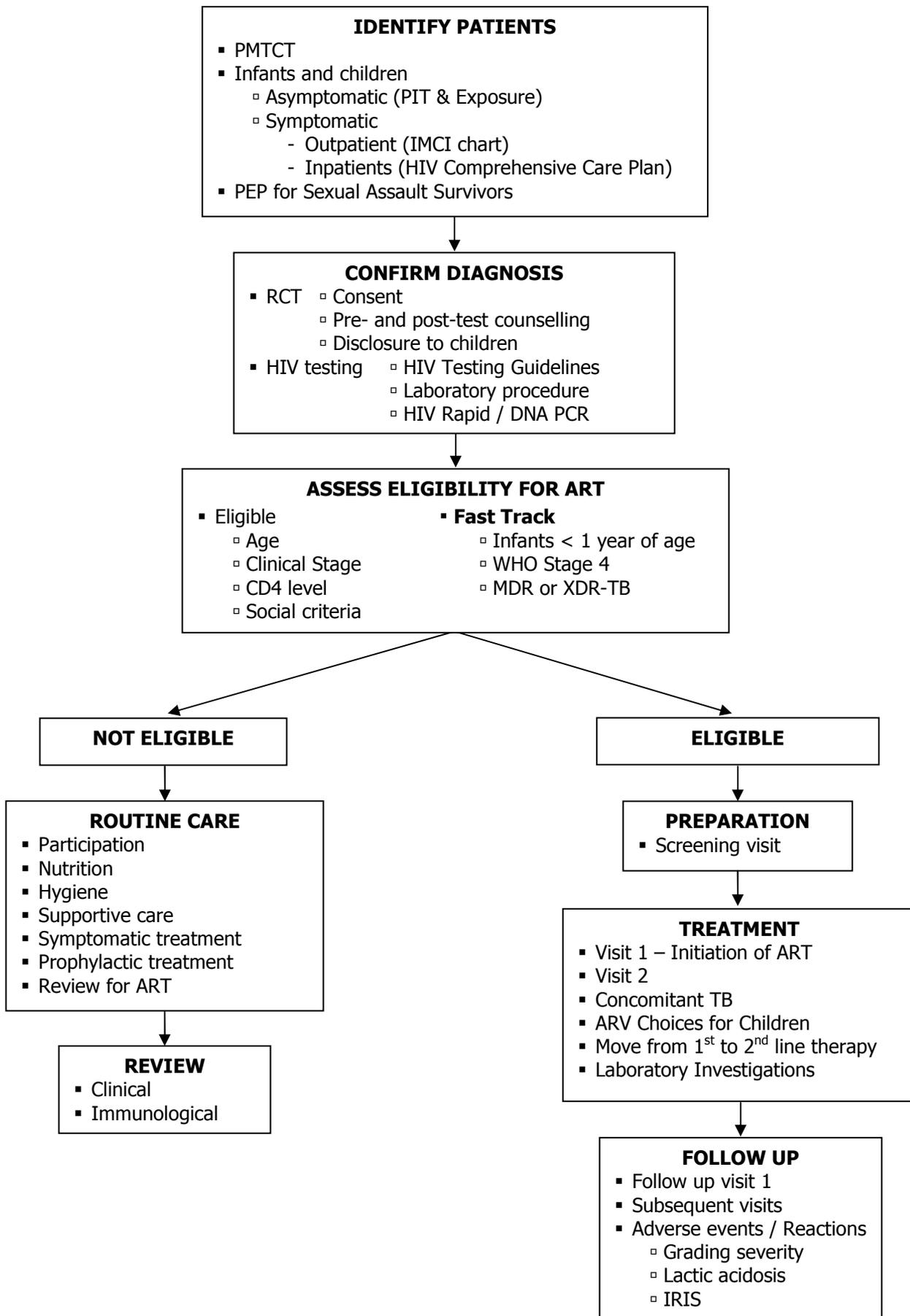
HEAD OF DEPARTMENT

DEPARTMENT OF HEALTH: KWAZULU-NATAL

TABLE OF CONTENTS

Paediatric ART Programme	3
Treatment Timeline	4
Identify Patients	5
HIV Counselling and Testing (HCT)	6
Confirm Diagnosis	7
HIV Blood Sample Requirements	9
Routine Care of HIV-Infected Children	10
Disclosure to Children	11
Caring for Care-givers	12
Assess Eligibility for ART	13
WHO Clinical Staging	14
Screening Visit	16
Excluding Tuberculosis	17
Antiretroviral Choices for Children	18
Treatment Visit 1	19
Treatment Visit 2	20
Laboratory Investigations	21
Follow up Visit 1	22
Subsequent Visits	23
Adolescent-Friendly HIV Services	24
Move from First to Second Line Therapy	25
Adherence Assessment	26
Adverse Drug Reactions	27
When, How and Where to Refer	30
Appendix I IMCI HIV Assessment Chart	33
Appendix II PMTCT National Guidelines	35
Appendix III HIV PEP following Sexual Assault	37
Appendix IV WHO Nutrition HIV Guidelines.....	38
Appendix V Developmental Assessment	40
Appendix VI Body Surface Area	42
Appendix VII Drug Profiles	43
Appendix VIII Simplified Dosing in Resource Poor Settings	53

PAEDIATRIC ART PROGRAMME



TREATMENT TIMELINE

The concept of a timeline for the process of initiation of ART for children is NOT to hinder access to therapy, but to enhance adherence to therapy. The timeline creates an additional means to monitor the care-giver's ability to adhere to a health programme. If s/he is unable to achieve the timeline, delay the initiation of ART until additional adherence training has occurred.

The timeline is a guide only and follow-up may need to be individualised for particular children.

Fast-Tracking

The following children must be fast-tracked for initiation of ART within 2 weeks:

- ALL children less than 1 year of age
- WHO Stage 4
- MDR or XDR tuberculosis

Time	Activity
	Identify patients (see pg 5)
	Confirm diagnosis (see pg 7-8)
	Assess eligibility for ART programme and assess for fast tracking (see pg 13)
- 2 weeks	Screening (see pg 16)
0 weeks	Treatment 1 (see pg 18)
2 weeks	Treatment 2 (see pg 19)
4 weeks	Follow up 1 (see pg 21)
8 weeks	Subsequent visits (see pg 22)
Monthly	To assess: <ul style="list-style-type: none"> ▫ Disease progression ▫ Growth monitoring ▫ Revision of drug dosages ▫ Adverse drug reactions
3 monthly	

IDENTIFY PATIENTS

It is essential that **every child** is assessed for signs of HIV infection **at every encounter** with the health system and that their care-givers are offered Provider Initiated Testing (PIT)

PMTCT PROGRAMME (see Appendix II)

Asymptomatic infants:

- HIV infection confirmed on routine HIV testing as part of the PMTCT programme
 - i.e. HIV DNA PCR
 - at 4 - 6 weeks of age, or
 - 4 - 6 weeks after cessation of breast feeding

Symptomatic infants:

- HIV disease is suspected on the basis of their clinical status

INFANTS & CHILDREN

Asymptomatic:

- PIT (Provider Initiated Testing)
- Screening children of **HIV-infected adults** through adult services:
 - CDC / Family Clinics

Symptomatic:

- Identification of children with one or more signs suggestive of HIV during routine clinic, OPD or hospital visits (see IMCI Chart in Appendix I for outpatients, and ensure an HIV Comprehensive Care Plan for inpatients)

SEXUAL ASSAULT POST EXPOSURE PROPHYLAXIS (PEP) (see Appendix III)

HIV-infected status is identified during the PEP programme for survivors of sexual assault.

HIV COUNSELLING AND TESTING (HCT)

Assent should be sought from all children
and if mature enough, the child should be included in the counselling process

CONSENT

Testing may only be done following pre-test counselling and informed consent with the following persons:

- the child, if of the age of 12 years and of sufficient maturity to understand the test
- the parent, legal guardian or care-giver of the child
- managers of children's homes, if child legally placed in the institution
- the medical superintendent of a hospital, in life-threatening situations

PRE-TEST COUNSELLING

- Choose a private area for counselling and assure the person of confidentiality
- Talk through the reasons for HIV testing – look at benefits and the disadvantages
- Find out how much the person knows and offer information about HIV and AIDS
- Offer information about the HIV antibody test, including information about the 'window period'
- Go through the implications of a positive test result, particularly if a parent has not been tested, as a positive result in the child suggests a positive result in the mother
- Discuss the person's possible responses to a positive test result. (Whom can he/she tell and where can s/he get support?)
- Be aware of the person's concerns and let these guide the discussion
- Go through the implications of a negative test result
- Provide information about how the test is done, and how to obtain results
- Give enough time for the person to consider whether s/he wants to have the test
- If the person decides to have the test, obtain consent in writing on the clinic card

POST-TEST COUNSELLING

Counselling after an HIV test is essential, irrespective of the result.

Test Results: (Remember that if an HIV ELISA/Rapid was done on an **infant** this will reflect the mother's status but not necessarily that of the child)

If the result is negative:

- Deal with the feelings arising from a negative result and explain about the 'window period'
- Discuss ways to prevent HIV infection, and the importance of remaining negative

If the result is positive:

- Tell the person as clearly and gently as possible, then deal with their immediate feelings
- Give the person time to understand and discuss the result, and to express emotion
- Provide information in a way that the person can understand
- Discuss how the person plans to spend the next few hours and days
- Identify what support s/he has and discuss disclosure issues with child and others
- Share information with the person about what to expect and how to care for the child
- Go through the ways the person can take care of her/his own health
- Encourage the person to ask questions
- Refer the person, where possible, to a community support organisation for follow-up
- Encourage the person to return for another follow up session
- If possible, write down some information to help the person remember what was said

CONFIRM DIAGNOSIS

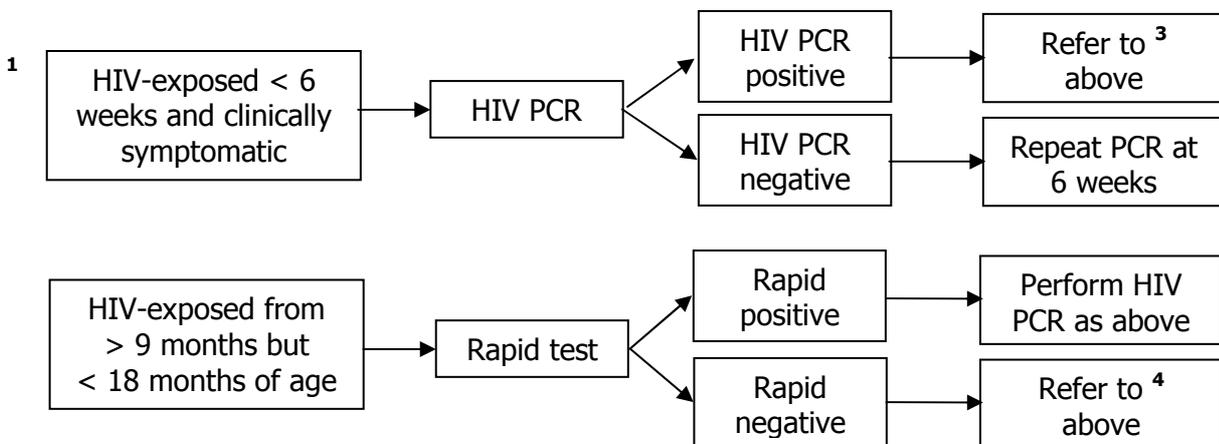
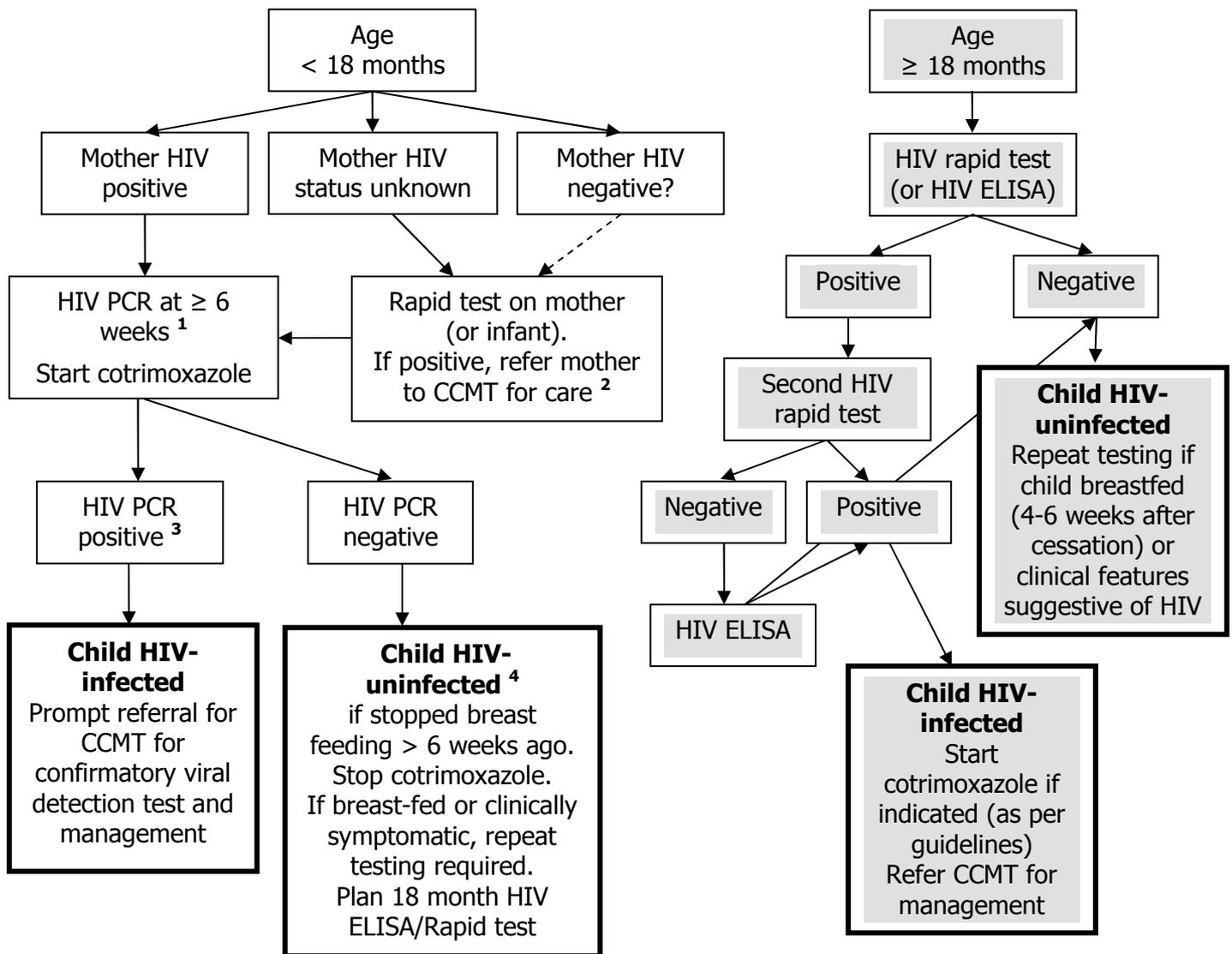
HIV TESTING GUIDELINES

Age	HIV testing	Positive Results	Negative Results
<18 months Do both tests	HIV antibody test: <ul style="list-style-type: none"> Rapid test <p>Not confirmatory if < 18 months</p>	<ul style="list-style-type: none"> Shows either mother's antibody or child's HIV antibody In first few months of life confirms child has been exposed to HIV, due to passive transfer of maternal antibodies Positive test results from 9-12 months of age usually suggests child is infected Indicates mother is infected and needs referral for ART eligibility 	<ul style="list-style-type: none"> If not breastfed = not infected If still breastfed = repeat test once breastfeeding is discontinued for 6 weeks or more Negative test result rules out infection acquired during pregnancy and delivery but child can still be infected through breastfeeding
	HIV virology tests: <ul style="list-style-type: none"> HIV DNA PCR (Dried Blood Spot) HIV RNA PCR (Viral Load) <p>Best performed ≥ 4 - 6 weeks of age</p> <p>Confirmatory test for < 18 months</p>	<ul style="list-style-type: none"> Positive virology test at any age = child is infected, i.e. <p>Positive HIV DNA PCR OR HIV RNA Viral load > 10 000 copies/ml</p>	<ul style="list-style-type: none"> Negative virology test and never breastfed, or not breast fed in the last 6 weeks = child is not infected Negative results if still breast feeding need to be confirmed 4 - 6 weeks or more after breast feeding discontinued
≥18 months	HIV antibody test: <ul style="list-style-type: none"> Rapid test (x2) HIV ELISA <p>Valid results as for adults</p>	<ul style="list-style-type: none"> Both Rapid tests positive = HIV infected child Do a confirmatory HIV ELISA if the two Rapid tests are discordant 	<ul style="list-style-type: none"> Negative = the child is not infected If negative and still breastfed, repeat test once breastfeeding discontinued for 6 weeks or more

Note: If at any point patient's clinical stage does not correlate with laboratory diagnosis please repeat test

HIV TESTING ALGORITHMS

(SA National DOH Guidelines 2010)



² Mother requires second rapid test to confirm her HIV positive status as soon as possible. At the same time she should receive clinical staging, CD4 count, TB screening, contraception advice and be advised that her partner and other children require HIV tests. Referral to Comprehensive Care Management and Treatment (CCMT) site: for ART if eligible or wellness clinic if not.

HIV BLOOD SAMPLE REQUIREMENTS

Test	Sample	Transport	Time Frame	
			To lab	Until results
Rapid HIV	Kit	Nil	-	20 mins
HIV DNA PCR (Dried blood spot)	<ul style="list-style-type: none"> ▪ Label card carefully ▪ Clean puncture area and allow to dry ▪ DO NOT squeeze/ milk puncture site ▪ DO NOT allow skin contact with the filter paper ▪ DO NOT touch the blood spots ▪ Ensure sufficient blood to fill the circles 	Dry for 3 hrs before placing in envelope	72 hrs	14 days
Elisa	Plain tube with gel (serum separator)	Room temperature	24 hrs	3 days
CD4	EDTA tube without gel	Room temperature	Same day	5 days
HIV Viral Load (HIV RNA PCR)	EDTA tube WITH gel (white or purple top)	Store at 4° C	24 hrs	4-6 wks
FBC	EDTA tube without gel	Room temperature	24 hrs	Same day
LFT(ALT) TG/Cholesterol	Plain tube (red top)	Room temperature	24 hrs	Same day
Glucose	Glucose tube (grey top)	Room temperature	24 hrs	Same day

ROUTINE CARE OF HIV-INFECTED CHILDREN

All HIV-infected children must be assessed for ART eligibility at every contact with the health services as well as being formally assessed for eligibility every 3 months (see IMCI Follow-Up Care Chart in Appendix I)

- **Participation**
 - In all decisions re- management of infection, implementation of these decisions and monitoring of wellbeing
 - Essential for adherence with programme and therapeutic regimens
 - Achieved by education and counselling
- **Nutrition**
 - Growth monitoring: weight, height and head circumference
 - Macronutrient supplements
 - Micronutrient supplements
 - Vitamin A
 - Multivitamins
 - De-worm with Albendazole every 6 months
- **Hygiene**
 - Aim to reduce exposure to micro-organisms to prevent mobilisation of white cells and reduce rate of replication of virus
 - Four areas of activity - personal, oral, food preparation and general environmental hygiene
- **Supportive care**
 - Immunisations
 - Avoid toxins, especially nicotine via 'passive smoking'
 - Balance exercise and rest
 - Reduce stress
- **Symptomatic treatment**
 - Early and appropriate treatment of all intercurrent infections
- **Prophylactic treatment**
 - Cotrimoxazole (see Appendix VIII)
 - Asymptomatic infants from 6 weeks until 1 year of age
 - All symptomatic children
 - If sensitivity to Cotrimoxazole, use Dapsone 1mg/kg daily (tablets can be crushed for younger children)
 - Cotrimoxazole can be stopped once child has been stable on ART for at least 6 months and has had two CD4 counts > 500 cells/mm³ (taken at least 3 months apart)
- **ART**
 - Assess eligibility for ART
 - Initiate ART if eligible
 - Reassess for eligibility regularly until eligible

DISCLOSURE TO CHILDREN

The aim of conversations with children should be to build a body of knowledge in the child around health, illness, medicines etc. that leads up to naming HIV, i.e. the point of disclosure. The purpose is to develop skills, knowledge and confidence in children as they grow up and continue care in the adult facilities.

This process should occur over a period of time and requires:

- **Time** for discussion with parents/care-givers and child during each visit
- Encouraging the formation of **support** groups at clinics to decrease social isolation
- **Patience**, as pushing the process before the family is ready may disrupt the therapeutic alliance and may have a negative impact on the ongoing care of the child
- **Not delaying the process too much as this may also have a negative impact on the child** (i.e. treatment refusal, poor school performance)

The first step is to find out what the child already knows (many know more than adults think). Conversations are dependent on the age and understanding (developmental level) of the child.

Age	Developmental Level	Aim	Disclosure
0 - 4 yrs NO DISCLOSURE YET	<ul style="list-style-type: none"> ▪ Depends on adults for all needs ▪ Needs comfort, support and security 	To build confidence of child in health workers and medicine taking	<ul style="list-style-type: none"> ▪ Allow child to be present throughout consultation ▪ Congratulate child on taking medicines well
5 - 7 yrs EARLY DISCLOSURE	<ul style="list-style-type: none"> ▪ Understands concrete ideas ▪ Can make links between medicine and well-being ▪ Based in present ▪ Interested in what will happen to them in the more immediate future 	To understand that medicines enable the body to keep well	<p>Child needs to be informed of illness and not necessarily HIV diagnosis.</p> <p>Concepts to be dealt with:</p> <ul style="list-style-type: none"> ▪ Good health and poor health - diet, cleanliness, exercise, healthy teeth ▪ Role of medicines - keep body healthy ▪ Infections as 'germs' that can hurt or damage the body ▪ The parts of the body that help keep infections away – the blood cells can be likened to soldiers defending a country
8 - 11 yrs PARTIAL DISCLOSURE	<ul style="list-style-type: none"> ▪ Is attending school ▪ Is able to hold ideas ▪ Can understand past, present and future 	To name the infection as HIV	<p>New concepts to discuss with child:</p> <ul style="list-style-type: none"> ▪ Germ is called a virus ▪ The germ can learn to hide from the medicines if the medicines are not taken regularly – resistance ▪ Name the virus as HIV ▪ Introduce idea of private information = disclosure to certain persons only
11 - 14 yrs FULL DISCLOSURE	<ul style="list-style-type: none"> ▪ Coping with school and friends ▪ Abstract thinking ▪ Increasing autonomy or independence ▪ Has begun puberty 	<p>Full knowledge of HIV infection is essential</p> <p>Build skills around negotiating own healthcare, sexual health and adult life</p>	<ul style="list-style-type: none"> ▪ Review adolescent's understanding of illness, medicines, health and HIV infection ▪ Ensure knowledge of sexuality and adolescent's rights (i.e. family planning, birth spacing) and responsibilities (i.e. prevention of STI's) ▪ Plan for future health care and ART

CARING FOR CARE-GIVERS

It is important to remember that successful and sustained administration of ART to (particularly young) children is dependent upon the agreement and support of their parents/care-givers. Attention must therefore be given to providing ongoing education and support for care-givers and ensuring that their own needs are identified and acted upon.

At every visit, you should assess the following:

1. Care-giver's health needs

Including care-giver's HIV status (plus CD4 count if indicated), TB status, mental (psychological) health, own current medications, understanding of own health conditions and adherence to own medications

2. Care-giver's financial needs

Ensuring that all appropriate grants are being obtained and the ability to meet transport costs to clinic

3. Care-giver's social needs

Including who else helps care for the child, number of dependents and adults in the household, access to clean water, electricity and sanitation

4. Care-giver's emotional needs

Including whom they obtain support from (including hospital support group if available) and family, friends, colleagues, faith-based or community-based organisations

5. Care-giver's learning needs

Including their understanding of HIV, ART, side effects and dosages, the importance of infection control, food hygiene, storage of ART, preparation of ORS and when to return to clinic (e.g. if a new symptom occurs)

6. Disclosure of diagnosis

Including level of understanding around diagnosis, ART etc. in the child, along with other family/friends who have been informed

Referrals

When referring to appropriate services to address identified needs, ensure that:

- ART visits for care-giver and child occur on the same day
- appointments for support services are on the same day as clinic visits

ASSESS ELIGIBILITY FOR ART

Patients must satisfy clinical and social criteria before being accepted for treatment

CLINICAL CRITERIA

- Confirmation of **diagnosis of HIV infection**

AND

- **All infants < 1 year of age**

OR

- **Children 1 - 5 years of age**
 - clinically WHO Stage 3 and 4, or
 - $CD4 \leq 25\%$, or
 - absolute CD4 count < 750 cells/mm³

OR

- **Children ≥ 5 years to 15 years of age**
 - clinically WHO Stage 3 and 4, or
 - absolute CD4 count < 350 cells/mm³

N.B. It is NOT necessary to wait for a CD4 result if the clinical criteria are met.

FAST TRACKING

The following patients require urgent initiation of ART **within 2 weeks** of becoming eligible:

- Infants < 1 year of age
- WHO Stage 4
- MDR or XDR-TB

SOCIAL CRITERIA

These criteria are extremely important for the success of the programme and need to be adhered to. The principle is that adherence to treatment must be at least probable.

The following are required:

- One identifiable care-giver able to supervise ART administration
- Disclosure to another adult in same household if possible who can assist with care
- Address social circumstances of vulnerable children to ensure they can receive treatment

REVISED WHO CLINICAL STAGING OF HIV & AIDS FOR INFANTS AND CHILDREN

Interim African region version for persons under 15 years of age with confirmed laboratory evidence of HIV infection (WHO, 2005), as appears in Guidelines for the Management of HIV in Children, 2nd Edition 2010, National Department of Health, South Africa

Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Stage 2

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart (human papilloma) virus infection
- Extensive molluscum contagiosum
- Fungal nail infections
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema (LGE)
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis or tonsillitis)

Stage 3

- Moderate unexplained malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more)
- Unexplained persistent fever (above 37.5°C intermittent or constant for longer than 1 month)
- Persistent oral candidiasis (after first 6 – 8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis or periodontitis
- Lymph node tuberculosis (axillary, cervical or inguinal)
- Pulmonary tuberculosis
- Symptomatic lymphoid interstitial pneumonitis (LIP)
- Severe recurrent bacterial pneumonia
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (< 8gm/dl), and/or neutropenia (< 500/mm³) and/or thrombocytopenia (< 50 000/mm³)

Stage 4

- Unexplained severe wasting, stunting or severe malnutrition not adequately responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infection (such as empyema, pyomyositis, bone or joint infection or meningitis, but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after one month of life)
- HIV encephalopathy
- Cytomegalovirus infection: retinitis or CMV infection affecting another organ, with onset at age older than one month
- Extrapulmonary cryptococcosis (including meningitis)
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated non-tuberculous mycobacterial infection
- Cerebral or B cell non-Hodgkin's lymphoma
- Progressive multifocal leukoencephalopathy (PML)
- HIV-associated nephropathy or HIV-associated cardiomyopathy
- HIV-associated rectovaginal fistula

SCREENING VISIT

1. Complete history and clinical evaluation

Check HIV result, and confirm or do post-test counselling if necessary

2. Document weight and height, and plot on growth charts
3. WHO Clinical Staging
4. Baseline Developmental Assessment

Using Appendix V, calculate the Developmental Quotient (DQ) as follows:

$$DQ (\%) = \frac{DA}{CA} \times 100$$

DA = (Fine motor age + Gross motor age +
Communication age + Personal/social age) ÷ 4, in months

CA = Chronological age, in months

5. Nutritional assessment (see Appendix IV)
6. Take blood for baseline HIV viral load and CD4 count (if not already available)
7. Take blood for FBC if starting an AZT-based regimen
8. Ensure that TB is adequately excluded (see pg 17)
9. Name the care-giver/s responsible for medication and make sure that this person is present during all discussion regarding antiretroviral therapy
10. Treatment literacy (over three sessions) to discuss Stigma and Disclosure; Healthy Living; and Adherence and Drug Readiness

If adherence by the family is questionable, they should be brought back for further adherence counselling/assessment until such time as the team feels that treatment can be commenced

EXCLUDING TUBERCULOSIS

Children at increased risk of TB disease include those:

- under 5 years of age
- with HIV infection
- with severe malnutrition

Exclude or confirm **active** TB based on the following assessment of history, clinical examination and special investigations

History

- TB contact
 - household contact with smear positive PTB
 - ongoing exposure to source case
- Chronic symptoms of TB
 - persistent, non-remitting cough > 2 weeks duration
 - documented weight loss or failure to thrive in the preceding 3 months
 - fatigue
 - persistent fever > 38°C for > 2 weeks
 - history of TB

Clinical examination

- Under nutrition
 - weight < 3rd centile or z-score < - 2
- Persistent neck masses
 - larger than 2 x 2 cm
 - not responding to antibiotics
 - no visible local cause
- Clinical signs of TB

Special investigations

- CXR suggestive of TB
- Mantoux Tuberculin skin test
- Bacterial confirmation

TB PREVENTIVE THERAPY (IPT)

TB prophylaxis is beneficial for all HIV-infected children, both on ART or not yet eligible for ART, provided that there is **no evidence of active TB** (see above assessment)

All HIV-infected children, with no signs or symptoms of active TB, must receive one course of TB preventive therapy (IPT) with INH

The recommended regimen for children is:

- Isoniazid (INH) 10 mg/kg/day continuously for 6 months
- Children on ART who start IPT must be carefully monitored as
 - D4T (Stavudine) and INH may increase risk of peripheral neuropathy, and
 - Nevirapine and INH may increase risk of hepatotoxicity

N.B. INH must be stopped immediately if there is any evidence of severe side effects

ANTIRETROVIRAL CHOICES FOR CHILDREN

The new NDOH regimens implemented from 1 April 2010 are shown in the table below

Children initiated on a D4T (Stavudine)-based regimen who are well must continue on that regimen.
Only children who develop toxicity to D4T (lipodystrophy, lactic acidosis, peripheral neuropathy or metabolic syndrome) and who are virologically suppressed should have D4T substituted with Abacavir.

Infants who were initiated on a Kaletra[®] based regimen must continue on that regimen even once they are over 3 years of age.

Initiation of ART	Birth to 3 years	Over 3 years and > 10 kg
1st Line	Abacavir (ABC) Lamivudine (3TC) Lopinavir/Ritonavir (LPV/r; Kaletra [®])	Abacavir (ABC) Lamivudine (3TC) Efavirenz (EFV; Stocrin [®])
2nd Line	Consult local referral centre*	Zidovudine (AZT) Didanosine (ddI) LPV/r (Kaletra [®])
If failing any 2nd line	Consult local referral centre*	Consult local referral centre*
For children on TB treatment	Abacavir (ABC) Lamivudine (3TC) ✧ Boosted LPV/r (Kaletra [®])	Abacavir (ABC) Lamivudine (3TC) Efavirenz (EFV; Stocrin [®])

* See back cover for referral centre details

✧ **Additional Ritonavir** to make Lopinavir/Ritonavir ratio 1:1 (see Appendix VII)

TREATMENT VISIT 1

1. History and clinical evaluation
2. Document weight and height, and update growth charts
3. Baseline Developmental Assessment and DQ, if not done previously (see Appendix V)
4. Check that growth and nutritional assessment has been done and the appropriate response implemented (see Appendix IV)
5. Check screening CD4 result (taken at first visit)
6. Identify the correct drug regimen
7. Take blood for baseline investigations if not done at screening visit
8. Review the importance of adherence and devices to assist adherence
9. Explain possible side effects of ART
10. Prescribe medication for 2 weeks
11. Issue pillboxes, syringes and diary cards, if available
12. Make a treatment plan with the parent or care-giver
13. Arrange adherence phone call in 1 week (if possible)
14. Arrange follow up visit after 2 weeks

TREATMENT VISIT 2

1. Adherence assessment (pill count and three day recall)
2. Reconcile returned empty containers with volume of medication prescribed since the last visit
3. Explain exact drug schedule for the child to the guardian, using the diary card
4. Adjust drug schedule if needed
5. Check all outstanding results
6. Issue pillboxes, syringes and diary cards, if available
7. Arrange follow up visit after 2 weeks

LABORATORY INVESTIGATIONS

Regimen	1 st Line		2 nd Line	
	ABC or D4T 3TC LPV/r	ABC or D4T 3TC Efavirenz	AZT ddI LPV/r	AZT ddI Efavirenz
-2 weeks (Screening) OR 0 weeks (Baseline)	CD4 count* Viral Load FBC ALT TG LDL-Cholesterol	CD4 count* Viral Load FBC ALT	CD4 count* Viral Load FBC ALT TG LDL-Cholesterol	CD4 count* Viral Load FBC ALT
1 month			FBC	FBC
2 months			FBC	FBC
3 months			FBC	FBC
6 months	CD4 count Viral Load TG LDL-Cholesterol	CD4 count Viral Load	CD4 count Viral Load FBC TG LDL-Cholesterol	CD4 count Viral Load FBC
12 months & then 12 monthly	CD4 count Viral Load TG LDL-Cholesterol	CD4 count Viral Load	CD4 count Viral Load FBC TG LDL-Cholesterol [♦]	CD4 count Viral Load FBC

* Repeat CD4 count ONLY if no result available in the past 1 month

♦ If TG or LDL-Cholesterol are abnormal, confirm with a **fasting** sample

FOLLOW UP VISIT 1

1. History and clinical evaluation
2. Document weight and height, and update growth charts
3. Adherence assessment (pill count and three day recall)
4. Reconcile returned empty containers with volume of medication prescribed since the last visit
5. Look for signs of toxicity or adverse reactions (see Adverse Drug Reactions on pg 26)
6. Review exact drug schedule for the child with the parent/guardian
7. Adjust drug schedule if needed
8. Do laboratory investigations as required (see Laboratory Investigations on pg 20)
9. Issue medication for 4 weeks
10. Issue pill boxes, syringes and diary cards where needed and available
11. Arrange follow up visit in 4 weeks

SUBSEQUENT VISITS

1. History and clinical evaluation
2. Document weight and height, and update growth charts
3. Monitor development and calculate the DQ every 6 months (see Appendix V)
Refer to nearest paediatric service if development static or regressing
4. WHO Clinical Staging
5. Screen for TB symptoms (see pg 16)
6. Adherence assessment (pill count and three day recall)
7. Reconcile returned empty containers with volume of medication prescribed since the last visit
8. Look for signs of toxicity or adverse reactions (Adverse Drug Reactions on pg 26)
9. Review exact drug schedule for the child with the parent/guardian
10. Adjust drug schedule if needed
11. Do laboratory investigations as required (see Laboratory Investigations on pg 20)
12. Issue medication for 4 weeks
13. Issue pill boxes, syringes and diary cards, if available
14. Arrange follow up visits (may be more often):
 - a. < 1 year of age monthly, until 1 year old
 - b. > 1 year of age monthly x 3 months,
then 3-monthly if stable (for growth assessment and dose adjustments)

ADOLESCENT-FRIENDLY HIV SERVICES

It is vital to develop adolescent-friendly services by identifying 'adolescent champions' in your facility who will drive the adolescent programme

- Adolescents (10 - 20 yrs) have different needs to those of children and adults
- Adolescent counselling needs to include accurate information around sexual and reproductive health and preparation for autonomy in adult services
- Adaptation of existing services to encourage continued engagement in healthcare is essential for the long-term health of the adolescent

Aim	Rationale	Actions
Full disclosure of HIV diagnosis	<ul style="list-style-type: none"> ▪ Facilitates appropriate preparation prior to transition to adult services ▪ Allows adolescent and care-giver opportunity for questioning and increased understanding and engagement 	<ul style="list-style-type: none"> ▪ Determine the adolescent's baseline knowledge of HIV ▪ Work towards full disclosure ▪ Encourage participation in care ▪ Use Step-by-Step Guide to Disclosure
Adolescent clinic day (i.e. promote peer support)	<ul style="list-style-type: none"> ▪ Peer support provides an opportunity for young people to share and learn ▪ Adherence to ongoing care is enhanced through continued support ▪ Relieves the burden of responsibility on healthcare staff 	<ul style="list-style-type: none"> ▪ Identify an 'Adolescent Champion' in your facility to lead developments ▪ Identify key learning objectives for adolescents and make them accessible ▪ Identify one day per week when young people (and their care-givers) will be seen together
Develop and implement an Adolescent Support Group	<ul style="list-style-type: none"> ▪ The needs of adolescents go beyond healthcare ▪ The opportunity to learn and share with peers is beneficial ▪ Adolescence poses challenges to adherence and accessing healthcare ▪ To engage adolescents and all relevant role players (i.e. adult and paediatric healthcare staff, NGOs, civil society) 	<ul style="list-style-type: none"> ▪ Identify key personnel ▪ Identify an appropriate venue ▪ Role players to agree on meeting schedule (day, time) ▪ Agree on structure, content and ground rules of the group (i.e. confidentiality) ▪ Promote shared ownership ▪ Consider provision of parallel care-giver support group
Enable smooth transition to adult clinic	<ul style="list-style-type: none"> ▪ Life-long adherence to ART is essential for achieving and maintaining optimal health 	<ul style="list-style-type: none"> ▪ Try to include someone from the Adult Clinic in the adolescent support group or adolescent clinic

MOVE FROM FIRST TO SECOND LINE THERAPY

Consider a move to second-line therapy under the conditions listed in the table below. For practical purposes, it is primarily the clinical features that are of importance.

N.B. Initiation of second-line therapy must only be undertaken after careful consideration and in consultation with the local referral centre

But before considering a change of regimen due to apparent ART failure, ensure that **adherence** has been good...

Clinical	Immunological	Virological
<p>Growth failure</p> <p>Loss of neuro-developmental milestones</p> <p>Disease progression</p> <ul style="list-style-type: none"> ▪ to additional disease in the current stage, or ▪ to next stage <p>Recurrence of prior opportunistic infections</p>	<p>Confirmed return of CD4 % to baseline</p> <p>More than 50% decline in CD4 % from peak</p>	<p>Persistent viral load of >1000 copies/ml, (i.e. two results taken three months apart)</p> <p>N.B. If the viral load is >1000 copies/ml, assess for any adherence issues, then repeat the viral load after three months</p> <p>For Adherence Assessment see table on following page</p>

ADHERENCE ASSESSMENT

Assess	Method	Intervention
Adherence	<ol style="list-style-type: none"> 1. Interview child and care-giver <ul style="list-style-type: none"> - 24 hour or 7 day recall - Description of: <ul style="list-style-type: none"> • WHO gives medication • WHAT is given (names/doses) • WHERE medications are kept • WHEN they are taken/given - Open-ended discussion re taking/giving medications 2. Review pharmacy records – timeliness of refills/pill-count 3. Observe medication administration: <ul style="list-style-type: none"> - Observe dosing/administration in clinic - Home-based observation - Hospital admission for trial of therapy 4. Psychosocial assessment: <p>Comprehensive family-focused assessment of factors likely to impact on adherence with particular attention to recent changes, i.e.</p> <ul style="list-style-type: none"> - Status of care-giver, financial stability, housing, relationships - School and achievements - Substance abuse - Mental health and behaviour - Childs and care-givers beliefs towards ARVs - Disclosure status 	<ul style="list-style-type: none"> ▪ Identify or re-engage family members to support/supervise adherence ▪ Estimate fixed daily times and routines for medicine administration ▪ Avoid confusion with drug names ▪ Explore opportunities for facility or home-based DOT ▪ Simplify regimen if feasible ▪ Substitute new agent if single agent is poorly tolerated ▪ Consider NGT or DOT treatment ▪ Utilisation of tools to simplify administration (pill boxes, reminders – alarms/cell phones) ▪ Address competing needs through appropriate social services ▪ Address and treat concomitant behavioral disorders ▪ Initiate disclosure discussions with family/child ▪ Consider need for child protection services and alternate care settings when necessary
Pharmacokinetics and dosing	<ol style="list-style-type: none"> 1. Recalculate doses of the individual drugs using weight and surface area 2. Identify concomitant medications including prescription, over-the-counter and recreational drugs 3. Assess for potential drug-drug interactions 4. Consider drug levels for specific ARV drugs 	<ul style="list-style-type: none"> ▪ Adjust drug doses ▪ Discontinue or substitute competing medications ▪ Reinforce applicable food restrictions

ADVERSE DRUG REACTIONS

ART commonly causes side-effects and occasionally serious adverse events (SAEs) can occur.

Mild side effects include:

- Mild nausea, vomiting, diarrhoea
- Dizziness; sleep disturbances (Efavirenz)
- General malaise
- Headache
- Peripheral neuropathy
- Nail discolouration

Generally, if patients experience mild side effects it is recommended that they continue treatment.

Grading the Severity of Paediatric Adverse Reactions (PACTG)

Laboratory Test Abnormalities (ULN = upper limit of normal)				
Item	Grade 1	Grade 2	Grade 3	Grade 4
Haemoglobin 3 months to 2 yrs	9.0 - 9.9 g/dL	7.0 - 8.9 g/dL	< 7.0 g/dL	Cardiac failure secondary to anaemia
Haemoglobin 2 years and over	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 x10 ⁹ /L	0.4 - 0.749 x10 ⁹ /L	0.25 - 0.399 x 10 ⁹ /L	< 0.25 x 10 ⁹ /L
ALT	1.25 - 2.5 x ULN	2.6 - 5.0 x ULN	5.1 - 10.0 x ULN	> 10.0 x ULN
Bilirubin	1.1 - 1.5 x ULN	1.6 - 2.5 x ULN	2.6 - 5.0 x ULN	> 5.0 x ULN
Triglycerides	-	1.54 - 8.46 mmol/L	8.47 - 13.55 mmol/L	> 13.56 mmol/L
LDL-Cholesterol	-	2.85 - 3.34 mmol/L	3.35 - 4.90 mmol/L	> 4.91 mmol/L

Clinical Adverse Events				
Item	Grade 1	Grade 2	Grade 3	Grade 4
Peripheral neuropathy	Diagnosis of peripheral neuropathy is difficult in children. Screen motor function against milestones and refer to specialist if peripheral neuropathy is suspected.			
Skin Rash / Dermatitis		Diffuse maculo-papular rash OR Dry desquamation	Vesiculation OR Ulcers	Exfoliative dermatitis OR Stevens-Johnson syndrome OR Erythema multiforme OR Moist desquamation

ACTION ON GRADING

Grades 1 and 2:

- Child remains on therapy
- Repeat the test
- Reassess clinically within 2 weeks

Grade 3:

- Test should be repeated within 1 week
- If still Grade 3, stop ALL antiretroviral drugs and seek expert specialist 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

General:

- Complete Adverse Event form
- Submit form to local pharmacy service

LIPODYSTROPHY

Lipodystrophy occurs in 18-33% of patients on ART, in association with a longer duration of therapy (> 1 year) and the use of D4T (Stavudine®), ddI (Didanosine®) and protease inhibitors.

HIV-associated lipodystrophy can present with:

- **Lipoatrophy** (fat loss): including facial fat loss with or without involvement of the buttocks and limbs = most common presentation
- **Lipohypertrophy** (fat accumulation): including increased fat around abdomen, buffalo hump and breast hypertrophy
- **Metabolic syndromes**: insulin resistance, hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia and low HDL levels. These individuals are at risk for Type 1 diabetes mellitus and coronary artery disease.

Monitoring:

1. Advise care-giver to report changes in facial features/body contours
2. Clinical examination for features of lipodystrophy
3. Anthropometry:
 - Waist-to-hip ratio
 - Abdominal circumference
 - Limb circumference
4. Radiology: Dual Energy X-ray Absorptiometry (DEXA scan) / MRI (Fat)

Management:

1. Early detection

To avoid irreversible lipoatrophy and permanent disfigurement look for:

- Facial wasting (lipoatrophy)
- Fat around abdomen or buffalo hump (lipohypertrophy)

2. Substituting D4T (Stavudine®)

- If undetectable viral load (< 50 copies/ml), D4T (Stavudine®) must be substituted with Abacavir
- If detectable viral load, consult local specialist center to decide on appropriate regimen

3. Treating lipodystrophy

- There are no established methods for treating lipodystrophy
- Encourage exercise and healthy diet to reduce fat accumulation
- Some patients improve if switched from a protease inhibitor to an NNRTI
- Statins and/or fibrates are effective at lowering cholesterol and triglyceride levels
- Insulin resistance can be improved with anti-diabetic agents

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

IRIS, or Immune Reconstitution Disease (IRD), is a paradoxical clinical deterioration despite good immunological and virological response to antiretroviral therapy. It is due to the improving immune system recognising and mounting an immune response to organisms that have infected the body during the early stages of HIV infection.

Causes:

A wide range of pathogens may induce IRIS including *Mycobacterium tuberculosis* (MTB), *Mycobacterium Bovis BCG*, *Herpes simplex virus*, *Mycobacterium avium complex*, *Mycobacterium leprae*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Aspergillus terreus*, *Candida albicans*, *Pneumocystis carinii*, CMV, JC virus, Human papilloma virus and Hepatitis B and C viruses (HBV, HCV).

Presentation:

- IRIS usually presents during the first 6 weeks after starting antiretroviral therapy
- Clinical presentations vary and depend on the causative organism and the organ system that is infected
- IRIS caused by MTB may present with high fever, lymphadenopathy, worsening of the original tuberculous lesion, and/or deteriorating chest X-ray features, including the development of a miliary pattern or pleural effusion

Management:

- Specific antimicrobial therapy to treat the underlying antigenic stimulus, e.g. TB treatment for IRIS caused by MTB
- In severe reactions, oral or intravenous corticosteroids and/or non-steroidal anti-inflammatory drugs (NSAID) can improve symptoms
- Temporary discontinuation of ART should only be considered in life-threatening severe reactions

WHEN, HOW AND WHERE TO REFER

- Looking after HIV-infected infants, children and adolescents requires many resources and skills
- Each patient and his/her family may need you to consult and refer to various services or different levels of care
- The province is divided into health districts within which there is a prescribed referral system to ensure patients and health care providers can access appropriate resources
- Familiarize yourself with your own referral system and local health and NGO resources
- All nursing, medical and support staff looking after children need ongoing training and support

When to refer	To whom	Where to refer
<p>Clinical reasons</p> <ul style="list-style-type: none"> ▪ Treatment failure: <ul style="list-style-type: none"> ▫ Clinical ▫ Immunological ▫ Virological ▪ Clinical course: <ul style="list-style-type: none"> ▫ Suspected IRIS ▫ Opportunistic infections ▫ Cannot explain clinical course ▪ Suspected adverse drug reaction 	<p>Senior clinician on-site</p> <p style="text-align: center;">↓</p> <p>Referral ART clinic</p> <p>(Consider telephonic consultation prior to transfer of patient)</p>	<ul style="list-style-type: none"> ▪ Area 1: King Edward VIII Hospital ▪ Area 2 : Edendale Hospital ▪ Area 3: Ngwelezana Hospital
<p>Pharmacological reasons</p> <ul style="list-style-type: none"> ▪ Drugs: <ul style="list-style-type: none"> ▫ Unsure of dose ▫ Drug interactions ▫ Side effects ▫ Storage & stability ▫ Poor taste (palatability) ▪ Drug supply: <ul style="list-style-type: none"> ▫ Availability 	<p>On-site senior clinician / ART pharmacist</p> <p style="text-align: center;">↓</p> <p>Referral centre ART clinicians / ART pharmacist</p> <p>ART Pharmacist</p>	<ul style="list-style-type: none"> ▪ Institution ▪ Referral centre ▪ District Pharmacist ▪ PPSD (Provincial Pharmaceutical Supply Depot)
<p>Nutrition (food-related) reasons</p> <ul style="list-style-type: none"> ▪ Child: <ul style="list-style-type: none"> ▫ Poor appetite ▫ Recurrent vomiting/reflux ▫ Poor weight gain ▫ Chronic/recurrent diarrhoea ▪ Family: <ul style="list-style-type: none"> ▫ Insufficient food ▫ Poor quality food 	<p>On-site senior clinician</p> <p style="text-align: center;">↓</p> <p>On-site dietician</p> <p style="text-align: center;">↓</p> <p>District nutritional services</p>	<ul style="list-style-type: none"> ▪ Local on-site ▪ District Office ▪ Provincial nutritional directorate

When to refer	To whom	Where to refer
<p>Laboratory results/bloods</p> <ul style="list-style-type: none"> ▪ Delay in getting results ▪ Incorrect results ▪ Confusing results ▪ Querying any result 	<p>NHLS staff</p> <p>Virology Department IALCH</p>	<ul style="list-style-type: none"> ▪ Manager - on-site NHLS laboratory ▪ Provincial NHLS (laboratories) ▪ Virology (IALCH)
<p>Social reasons</p> <ul style="list-style-type: none"> ▪ Poor adherence ▪ Financial problems at home ▪ Child care problems at home 	<p>Counsellor / sister in ART clinic</p> <p>Social worker</p>	<ul style="list-style-type: none"> ▪ On-site ART clinic ▪ On-site Social worker ▪ Dept Population Development & Social Welfare ▪ NGO sector
<p>Accessing grants</p> <ul style="list-style-type: none"> ▪ Child Support Grant <ul style="list-style-type: none"> ▫ Poverty alleviation ▪ Foster Care Grant <ul style="list-style-type: none"> ▫ Surrogate care placement ▪ Care Dependency Grant <ul style="list-style-type: none"> ▫ Disability 	<p>Social worker</p>	<ul style="list-style-type: none"> ▪ Social Worker on-site ▪ Dept Population Development & Social Welfare (Call centre: 033-264 3000/1/2/3/4) ▪ SASSA
<p>Developmental reasons</p> <ul style="list-style-type: none"> ▪ Problems with hearing ▪ Problems with vision ▪ Gross motor problems ▪ Fine motor problems hand-eye co-ordination ▪ General developmental delay ▪ Poor or abnormal interaction with family and peers 	<p>Supplementary health services:</p> <ul style="list-style-type: none"> ▪ OT ▪ Physiotherapist ▪ Audiologist ▪ Psychologist <p>Specialist services</p>	<ul style="list-style-type: none"> ▪ Local services <ul style="list-style-type: none"> ▫ On-site ▫ Within district ▪ Regional Hospital <ul style="list-style-type: none"> ▫ Supplementary health services ▫ Paediatric Dept ▫ Other disciplines
<p>Educational problems</p> <ul style="list-style-type: none"> ▪ School refusal ▪ Poor performance ▪ Problems with attention ▪ Problems with disclosure ▪ Missing school too often 	<p>Counsellor in clinic</p> <p>Senior clinicians</p> <p>OT</p> <p>Psychologist</p>	<ul style="list-style-type: none"> ▪ On-site ▪ District office ▪ Regional Hospital ▪ Dept of Education (SNES)

THEN CONSIDER HIV INFECTION

Has the child been tested for HIV infection?

IF YES, ASK:

- What was the result?
- If the test was positive, is the child on ART?
- If the test was negative, was the child still breastfeeding at the time that the test was done, or had the child been breastfed in the six weeks before the test was done? Is the child still breastfeeding?

HIV testing in children:

- Below 18 months of age, use an HIV PCR test to determine the child's HIV status. Do not use an antibody test to determine HIV status in this age group.
- 18 months and older, use an rapid (antibody) test to determine HIV status. If the rapid test is positive then it should be repeated. If the second test is positive, this confirms HIV infection (in a child older than 18 months). If the second test is negative, refer for ELISA test and assessment.

NOTE:

All children who have had a PCR test should have an HIV antibody test at 18 months of age.

Classify
for HIV infection in
the child

<ul style="list-style-type: none"> • Positive HIV test in child. or <ul style="list-style-type: none"> • Child on ART. 	CONFIRMED HIV INFECTION	<ul style="list-style-type: none"> ➢ All children must be assessed for possible ART. Children younger than 12 months must be referred to an ART site. Children older than one year can be assessed at the clinic or be referred. ➢ Give cotrimoxazole prophylaxis from 6 weeks (p. 9) ➢ Assess feeding and counsel appropriately (p. 19-22) ➢ Ask about the mother's health, provide VCT where appropriate and refer if necessary ➢ Provide long term follow-up (p. 28)
<ul style="list-style-type: none"> • Negative HIV test. and • Child still breastfeeding or stopped breastfeeding less than 6 weeks before test was done. 	POSSIBLE HIV INFECTION	<ul style="list-style-type: none"> ➢ If mother is HIV positive, give cotrimoxazole prophylaxis from 6 weeks (p. 9) ➢ Assess feeding and counsel appropriately (p. 19-22) ➢ Repeat HIV testing 6 weeks after stopping breastfeeding to confirm HIV status ➢ Provide follow-up care (p. 28)
<ul style="list-style-type: none"> • Negative HIV test. and • Child no longer breastfeeding (stopped at least six weeks before test was done). 	HIV NEGATIVE	<ul style="list-style-type: none"> ➢ Consider other causes if child has features of HIV infection ➢ Provide routine care

If no test result available, check for features of HIV

ASK:

- Has the mother had an HIV test? If YES, was it negative or positive?

FEATURES OF HIV INFECTION

ASK:

- Does the child have PNEUMONIA now?
- Is there PERSISTENT DIARRHOEA now or in the past three months?
- Has the child ever had ear discharge?
- Is there low weight?
- Has weight gain been unsatisfactory?

LOOK and FEEL:

- Any enlarged lymph glands in two or more of the following sites - neck, axilla or groin?
- Is there oral thrush?
- Is there parotid enlargement?

Classify

<ul style="list-style-type: none"> • 3 or more features of HIV infection. 	SUSPECTED SYMPTOMATIC HIV INFECTION	<ul style="list-style-type: none"> ➢ Give cotrimoxazole prophylaxis (p. 9) ➢ Counsel and offer HIV testing for the child ➢ Counsel the mother about her health, offer VCT if appropriate and refer if needed ➢ Assess feeding and counsel appropriately (p. 19-22) ➢ Provide long-term follow-up (p. 28)
<ul style="list-style-type: none"> • Mother HIV positive 	HIV EXPOSED	<ul style="list-style-type: none"> ➢ Give cotrimoxazole prophylaxis (p. 9) - unless child is older than one year and clinically well ➢ Counsel and offer HIV testing for the child ➢ Counsel the mother about her health, and refer if needed ➢ Assess feeding and counsel appropriately (p. 19-22) ➢ Provide long-term follow-up (p. 28)
<ul style="list-style-type: none"> • One or two features of HIV infection 	POSSIBLE HIV INFECTION	<ul style="list-style-type: none"> ➢ Counsel and offer HIV testing for the child ➢ Counsel the mother about her health, offer VCT if appropriate and refer if needed ➢ Reclassify the child based on the test results
<ul style="list-style-type: none"> • No features of HIV infection 	HIV INFECTION UNLIKELY	<ul style="list-style-type: none"> ➢ Provide routine care.

GIVE FOLLOW-UP CARE

CONFIRMED HIV INFECTION on ART

Children who are stable on ART will be referred to clinic level. They should be seen monthly and the following care should be provided:

- Routine child health care: immunization, growth monitoring, feeding assessment and counselling and developmental screening.
- Check for adherence.
- Check for ARV side effects.
- Check for opportunistic infections or other problems.
- Provide ARVs and cotrimoxazole prophylaxis (p. 9).
- **Refer if:** ulcerating skin rash, side effects, poor response to treatment, or any other problems which can not be dealt with at the clinic.

POSSIBLE HIV INFECTION

See the child at least once every month. At each visit provide:

- Routine child health care: immunization, growth monitoring, and developmental screening.
- Feeding assessment and counselling to ensure that the mother is practising exclusive feeding (breast or replacement).
- Cotrimoxazole prophylaxis (p. 9).
- Assessment, classification and treatment of any new problem.
- Recheck child's HIV status 6 weeks after cessation of breastfeeding. Reclassify the child according to the test result.
- Ask about the mother's health. Provide counselling, HIV testing and referral if necessary.

HIV EXPOSED

See the child at least once every month. At each visit provide:

- Routine child health care: immunization, growth monitoring, and developmental screening.
- Feeding assessment and counselling to ensure that the mother is practising exclusive feeding (breast or replacement).
- Cotrimoxazole prophylaxis (p. 9).
- Assessment, classification and treatment of any new problem.
- Test the child at six weeks (PCR), and reclassify according to the test results.
- Retest the child six weeks after cessation of breastfeeding. Reclassify the child according to the test result.
- Ask about the mother's health. Provide counselling and referral if necessary.

CONFIRMED HIV INFECTION not on ART

All children less than one year of age should have a CD4 count done and should be referred to an ART site for assessment for possible ART. If these children are referred back to the clinic, they should be followed up monthly.

Those older than one year should be assessed at the clinic for ART eligibility (using CD4 count and clinical criteria). Those meeting the criteria should be referred. Those not meeting the criteria can be followed up at the clinic (at least three monthly).

The following should be provided at each visit:

- Routine child health care: immunization, growth monitoring, feeding assessment and counselling and developmental screening.
- Cotrimoxazole prophylaxis (p. 9).
- Assessment, classification and treatment of any new problem.
- Staging and possible referral for ART (children should be staged clinically and with CD4 counts at least six monthly to see if they meet the criteria for ART treatment).
- Ask about the mother's health. Provide VCT and referral if necessary.

SUSPECTED SYMPTOMATIC HIV INFECTION

Children with this classification should be tested, and reclassified on the basis of their test result.

See the child at least once a month. At each visit:

- Provide routine child health care: immunization, growth monitoring, feeding assessment and counselling, and developmental screening.
- Provide Cotrimoxazole prophylaxis from 6 weeks of age (p. 9).
- Assessment, classification and treatment of any new problem.
- Ask about the mother's health. Provide VCT and referral if necessary.

APPENDIX II

PMTCT NATIONAL GUIDELINES (April 2010)

- 1 in 3 babies born to HIV-infected mothers will be infected with HIV during pregnancy, delivery and via breast milk, without intervention
- PMTCT can reduce transmission to less than 2%
- Don't forget the father – prevention and/or treatment of HIV infection; planning for parenthood

All mothers must be offered HIV testing and counseling at the **first** ante-natal visit and HIV + mothers must be clinically staged and offered a CD4 test at the same visit

THE MOTHER

- It is very important to discuss feeding choice with the mother, as follows:
 - **Breastfeeding is the feeding option of choice for all infants, including HIV exposed infants**
 - Mothers should be encouraged to breastfeed with infant NVP prophylaxis for up to 12 months (including exclusive breastfeeding with appropriate weaning to solid food and breastfeeding at 4-6 months)
 - Mothers who are unable to breastfeed and meet the AFASS criteria should be counselled on safe and appropriate formula feeding (NB: Formula feed will no longer be provided as part of the PMTCT programme)

MATERNAL REGIMENS	
Currently on lifelong ART	Continue ART Substitute EFV with NVP if in first 12 weeks of pregnancy
Eligible for lifelong ART (i.e. CD4 ≤ 350 or clinical stage 3 or 4)	Tenofovir (TDF) + 3TC/ Emtricitabine (FTC) + NVP Start lifelong ART within 2 weeks (Use AZT instead of TDF, + 3TC + NVP, if renal disease)
For MTCT prophylaxis (i.e. not eligible for ART as CD4 > 350)	AZT from 14 weeks sdNVP at onset of labour + AZT 3 hrly during labour Single dose of TDF + FTC (Truvada [®]) during labour
Unbooked and presents in labour	sdNVP at onset of labour + AZT 3 hrly during labour Single dose of TDF + FTC (Truvada [®]) during labour Assess for ART eligibility before discharge

THE BABY

- All HIV-exposed babies must have a HIV DNA PCR
 - at 4 - 6 weeks of age (preferably during their routine 6 week immunization visit), or
 - 4 - 6 weeks after cessation of breast feeding
- All HIV DNA PCR positive babies must be referred as soon as possible to their nearest treatment centre to initiate ART – do **not** wait for a CD4 or viral load result
- Cotrimoxazole prophylaxis should be started from 6 weeks (2.5 ml daily)
- Immunisation should be given according to SA EPI schedule, unless baby has signs of AIDS

INFANT REGIMENS		
Mother on lifelong ART	NVP at birth and then daily for 6 weeks irrespective of infant feeding choice	<p style="text-align: center;">NVP dose</p> <p>Birth to 6 wks (< 2.5 kg) 10 mg/day (1 ml)</p> <p>Birth - 6 wks (> 2.5 kg) 15 mg/day (1.5 ml)</p> <p>6 wks - 6 months 20 mg/day (2 ml)</p> <p>6 - 9 months 30 mg/day (3 ml)</p> <p>9 months to end of breast feeding 40 mg/day (4 ml)</p>
Mother on AZT for MTCT prophylaxis	NVP at birth and then daily for 6 weeks, continued as long as any breastfeeding	
Mother HIV-infected and no MTCT prophylaxis	NVP at birth and then daily for 6 weeks, continued as long as any breastfeeding Assess mother for ART eligibility within 2 weeks	
Unknown maternal status, orphaned or abandoned	HIV Ab test immediately If baby HIV Ab + (i.e. HIV-exposed), give NVP immediately and then daily for 6 weeks, continued as long as any breastfeeding Follow up 6 week HIV DNA PCR	
All exposed infants who are exclusively formula fed can stop NVP at 6 weeks		

APPENDIX III

HIV PEP FOLLOWING CHILDHOOD SEXUAL ASSAULT

- The diagnosis of childhood sexual assault is based on what children report, NOT on the basis of clinical features identified on examination.
- All children with **suspected** sexual assault MUST be offered post exposure prophylaxis in the following circumstances:
 - suspicion of penetrative abuse
 - presentation within 72 hours of abuse
 - > 18 months of age: HIV negative status i.e. HIV rapid negative
 - < 18 months of age: cover with PEP until PCR result available. If PCR is +ve discontinue PEP; if PCR is -ve, continue PEP for full 28 days
- Counselling must cover risk of HIV following sexual assault, availability of ART, possible benefits of ART
- May need to obtain "superintendent's" consent for testing as this must be seen as potentially life threatening

Regimens

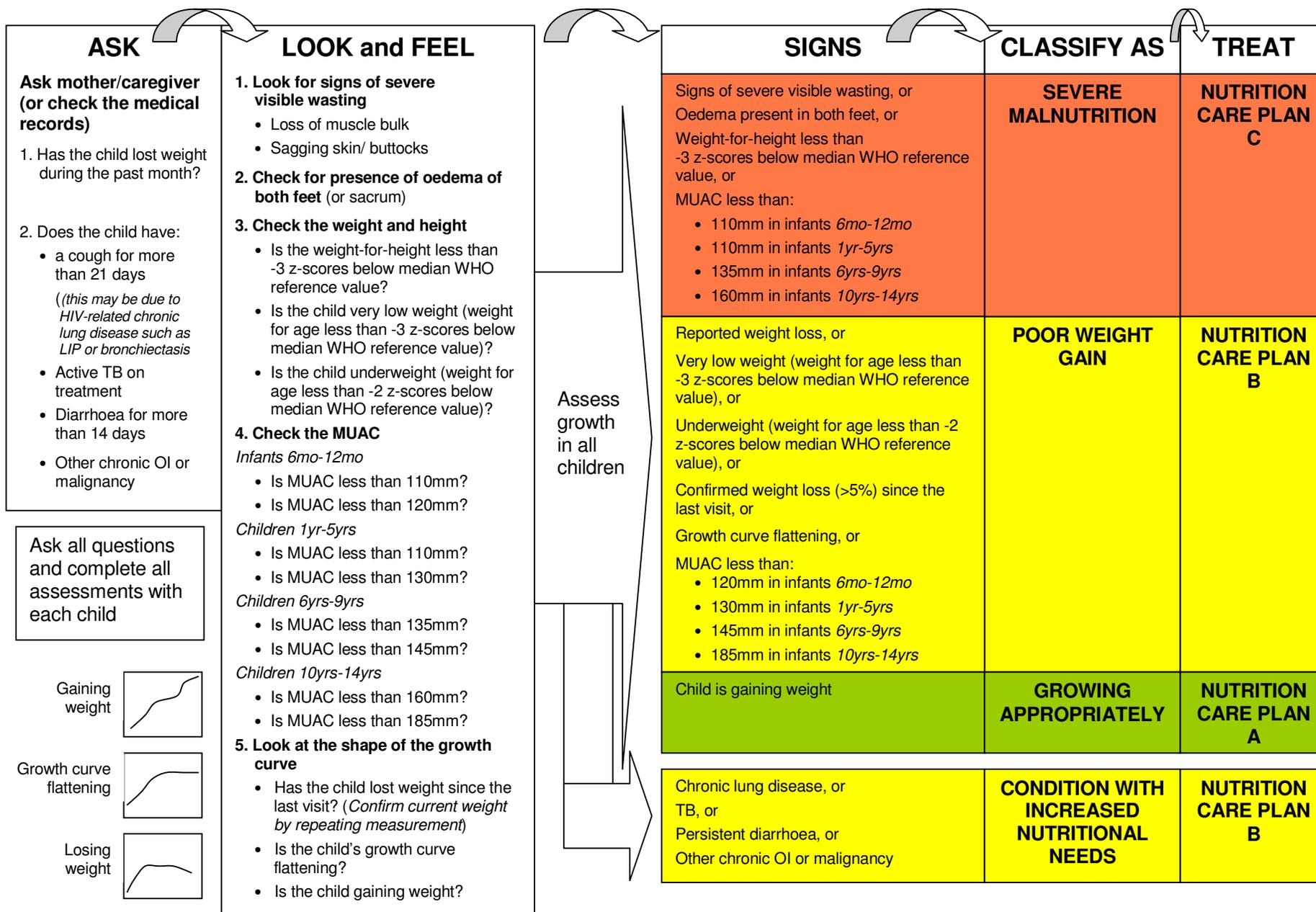
- *Basic regimen*
AZT & 3TC for 28 days
Dispense the full course at the first visit as compliance with follow up is generally poor
- *Expanded regimen*
Add Kaletra in all high risk cases namely where there has been:
 - a breach of skin or mucosal surface
 - anal penetration
 - multiple perpetrators

Drugs must be pre-packed and available according to the age of the child (see table below)

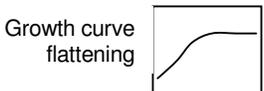
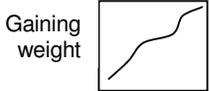
Age	AZT (12 hrly)	3TC (12 hrly)	Kaletra (12 hrly)
< 3 months	4.0 ml	1.0 ml	1.0 ml
3 months	5.0 ml	2.0 ml	1.5 ml
6 months	5.0 ml	3.0 ml	1.5 ml
9 months	5.0 ml	3.5 ml	2.0 ml
12 months	7.5 ml	4.0 ml	2.0 ml
18 months	7.5 ml	4.5 ml	2.0 ml
2 years	10.0 ml	5.0 ml	2.0 ml
3 years	10.0 ml	5.5 ml	2.0 ml
4 years	1 capsule	6.5 ml	2.5 ml
5 years	1 capsule	7.0 ml	2.5 ml
6 years	1 capsule	8.0 ml	2.5 ml
7 years	½ tablet	9.0 ml	3.0 ml
8 years	½ tablet	10.0 ml	3.0 ml
9 years	½ tablet	11.0 ml	3.5 ml / 1½ tablets*
10 years	½ tablet	12.5 ml	3.5 ml / 1½ tablets*
11 years	2 capsules	14.0 ml	4.0 ml / 1½ tablets*
12 years	2 capsules	1 tablet	4.0 ml / 1½ tablets*
13 years	2 capsules	1 tablet	5.0 ml / 2 tablets

* best achieved by giving: tablets in the morning and 1 tablet at night

MUAC = mid-upper-arm circumference



Ask all questions and complete all assessments with each child



Steps	Nutrition Plan A <i>for the child growing well ± ART</i>	Nutrition Plan B <i>for the child with poor weight gain or increased nutritional needs</i>	Nutrition Plan C <i>for the severely malnourished HIV-infected child</i>
1	Ask about general condition of child	Clinically stage child and assess for ART If on ART, assess response (clinical & imm.)	Assess if child needs to be admitted ("Danger Signs"). If not, for manage at home
2	Check mother's health (and need for ART) and care of other children	Check mother's health (and need for ART) and care of other children	Clinically stage child and assess for ART If on ART, assess response (clinical & imm.)
3	Nutrition counselling	Nutrition counselling	Check mother's health (and need for ART) and care of other children
4	Feeding: provide 10% additional energy	Feeding: provide 20-30% additional energy	Feeding: provide 50-100% additional energy
5	Ensure adequate micronutrient intake: Vidaylin drops or Multivitamin syrup	Ensure adequate micronutrient intake: Vidaylin drops or Multivitamin syrup Add Zinc (20 mg daily x 2 weeks) if recent DD	Ensure adequate micronutrient intake: Vidaylin drops or Multivitamin syrup Add Zinc (20 mg daily x 4 weeks) if recent DD
6	Vitamin A supplements every 6 months: < 6 mths 50,000 IU 6-12 mths 100,000 IU 1-5 yrs 200,000 IU > 5 yrs Vit A part of daily micronutrient suppl.	Vitamin A supplements every 6 months: < 6 mths 50,000 IU 6-12 mths 100,000 IU 1-5 yrs 200,000 IU > 5 yrs Vit A part of daily micronutrient suppl.	Vitamin A supplements every 6 months: < 6 mths 50,000 IU 6-12 mths 100,000 IU 1-5 yrs 200,000 IU > 5 yrs Vit A part of daily micronutrient suppl.
7	De-worm every 6 months: Albendazole (oral) 400 mg single dose every 6 months after first year of life	De-worm every 6 months: Albendazole (oral) 400 mg single dose every 6 months after first year of life	De-worm every 6 months: Albendazole (oral) 400 mg single dose every 6 months after first year of life
8	Cotrimoxazole prophylaxis: Provide from 6 weeks of age at 5 mg/kg/day Alternative: Dapsone 1 mg/kg/day	Cotrimoxazole prophylaxis: Provide from 6 weeks of age at 5 mg/kg/day Alternative: Dapsone 1 mg/kg/day	Cotrimoxazole prophylaxis: Provide from 6 weeks of age at 5 mg/kg/day Alternative: Dapsone 1 mg/kg/day
9	Ensure mother/caregiver understands care plan and ask if s/he has any questions	Ensure mother/caregiver understands care plan and ask if s/he has any questions	Ensure mother/caregiver understands care plan and ask if s/he has any questions
10	Review in 2-3 months	Review visit 1-2 weeks, then every 1-2 months	Review every week

Note: Please use the table below to adapt the z-scores contained in the WHO Nutritional Assessment for local use

Weight-for-height		Weight-for-age	
-1 z-score	91 - 93 % expected median weight-for-height	-1 z-score	86 - 89 % expected median weight-for-age
-2 z-score	84 - 86 % expected median weight-for-height	-2 z-score	76 - 80 % expected median weight-for-age
-3 z-score	77 - 79 % expected median weight-for-height	-3 z-score	66 - 72 % expected median weight-for-age

DEVELOPMENTAL MILESTONES

Age	Gross motor	Fine motor	Communication	Personal/social
3 months	Pull to sit: no head lag Prone: support on forearm lifts head buttocks flat Rolls over	Follows through 180° Hands open Holds object placed in hand Watches hands Pulls at clothes	Coos & chuckles Quietens to familiar sound Turns head towards sound	Excited when fed Reacts to familiar situation
6 months	Pull to sit: braces shoulders pulls to sit Prone: extended arms lifts head & chest Supine: plays with feet Sits with support	Reaches for object Radial approach to toys Transfers Shadow reaction in other arm	Babbles Repetition Laughs aloud Turns to mother's voice	Puts everything in mouth Responds to image in mirror Starts to hold bottle Shows likes & dislikes
9 months	Sits without support Rolls Crawls Rocks on all fours Pulls to stand	Holds a cube in each hand Points	Deliberate vocalisation Babbles Imitates sounds Understands "no" / "bye-bye"	Stranger anxiety Holds bottle Drinks from cup
12 months	Bear creep Walks around furniture sideways Walks with feet apart & arms up	Pincer grasp Releases on request Begins to cast Looks for toy when out of sight	Knows own name 2 - 3 words with meaning Understands simple commands	Finger feeds Pushes arms into sleeves Plays games
15 months	Walks alone Collapses backwards Stairs: creeps up, goes down backwards	2 cube tower Holds 2 cubes in one hand	Jabbers with expression 2 - 6 words Points to objects on request	Picks up, drinks & puts down cup Spoon feeds with a mess Indicates wet nappy

Age	Gross motor	Fine motor	Communication	Personal/social
18 months	Walks with arms down Cannot turn unless still Pulls a toy Throws a ball Climbs onto chair	3 cube tower Scribbles	6 - 20 words	Handles spoon well Looks at pictures Takes off shoes & socks
24 months	Runs Stairs: up & down 2 feet per step Kicks a ball Squats & rises without hands	6 cube tower Obvious hand preference	~ 50 words Short phrases Asks for food, drink, toilet	Spoon feeds without mess Clean & dry by day Pretend play
36 months	Rides tricycle Stairs: up - 1 foot per step down - 2 feet per step Climbs Walks on tiptoes Throws & kicks ball	9 cube tower Copies circle Cuts with scissors Builds a bridge	Knows name & sex Uses pronouns Talks incessantly	Toilet trained Dresses with supervision Eats with a fork Washes & dries hands
48 months	Stairs: up & down 1 foot per step Stands on 1 leg for 3 – 5 seconds Hops	Copies cross Builds gate	Full name & age Recognizes colours	Eats with spoon & fork Dresses & undresses Make believe play Always asking questions
60 months	Walks along narrow line Hops on each foot separately	6 cube steps Copies square & triangle Draws a man	Fluent speech Knows 3 opposites	Dresses & undresses alone Uses knife & fork Chooses own friends
72 months	Sits up without using hands Walks backwards along straight line	10 cube steps Copies diamond	Learns comparatives	Cooperative play

Adapted from Kibel and Wagstaff, *Child Health for All*, 2nd ed. Cape Town: Oxford University Press, 1995.

APPENDIX VI

ESTIMATION OF BODY- SURFACE AREA IN INFANTS AND CHILDREN

$$\text{Body surface area BSA} = \sqrt{\frac{\text{Ht(cm)} \times \text{Wt(kg)}}{3600}} \text{ m}^2$$

Body Weight (kg)	Surface Area (m ²)
2	0.16
2.5	0.19
3	0.21
3.5	0.24
4	0.26
4.5	0.28
5	0.3
5.5	0.32
6	0.34
6.5	0.36
7	0.38
7.5	0.4
8	0.42
8.5	0.44
9	0.46
9.5	0.47
10	0.48

Body Weight (kg)	Surface Area (m ²)
11	0.53
12	0.56
13	0.59
14	0.62
15	0.65
16	0.68
17	0.71
18	0.74
19	0.77
20	0.79
21	0.82
22	0.85
23	0.87
24	0.9
25	0.92
26	0.95
27	0.97
28	1.0
29	1.0
30	1.1

Body Weight (kg)	Surface Area (m ²)
31	1.1
32	1.1
33	1.1
34	1.1
35	1.2
36	1.2
37	1.2
38	1.2
39	1.3
40	1.3
41	1.3
42	1.3
43	1.3
44	1.4
45	1.4
46	1.4
47	1.4
48	1.4
49	1.5
50	1.5

Standardised doses are provided in increments of 0.05m².
Therefore, identify the surface area from the weight on the above table, then **round up**
to calculate the actual dose
e.g. weight 25 kg = SA 0.92 m² , then round up to 0.95m² .

Source: UKCCSG

INTRODUCTION TO ARV DRUG PROFILES

- ✓ The aim is to move from syrup to capsules/tablets as soon as possible
- ✓ Drug dose is determined by the size of the child, but the ability to swallow by age or maturity, and learning to swallow may require careful coaching by a neutral trainer
- ✓ It is important that a child stay on syrups until s/he is comfortable swallowing capsules and tablets, which usually occurs around 6 years of age
- ✓ When dispensing tablets that need to be halved, provide a tablet cutter if possible
- ✓ Remember that HIV-infected children tend to have poor growth and are therefore small for age
- ✓ An adolescent should be changed to the adult regimen when s/he reaches Tanner stage 3 or more

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

- Abacavir (ABC; e.g. Ziagen[®])
- Didanosine (ddI; e.g. Videx[®])
- Lamivudine (e.g. 3TC[®])
- Stavudine (D4T; e.g. Zerit[®])
- Zidovudine (AZT; e.g. Retrovir[®])

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- Efavirenz (EFV; e.g. Stocrin[®])
- Nevirapine (NVP; e.g. Viramune[®])

Protease Inhibitors

- Lopinavir/Ritonavir (LPV/r; e.g. Kaletra[®], Aluvia[®])
- Adjusted Kaletra[®] or Aluvia[®] dosing for children on TB treatment

Abacavir (ABC; Ziagen[®])

Dose:

8 mg/kg/dose

Frequency:

12 hourly

Formulation:

Syrup - 20 mg/ml

Tablets - 300 mg

Comments:

- Can administer with food
- **Hypersensitivity reaction** (with or without rash) can be fatal
- Re-challenge is contra-indicated in any patient who has had hypersensitivity reaction
- Do not stop Abacavir unless advised by doctor

Side effects:*Common*

Headache

Nausea and vomiting

Diarrhoea

*Rarer***Hypersensitivity reaction**

Usually in first 6 weeks after initiation of treatment with ABC

Clinical features:

- fever
- maculopapular rash
- nausea, vomiting, diarrhoea
- fatigue
- pharyngitis
- dyspnoea, cough

Lab findings:

- ↑ ALT, ↑ CK
- Lymphopaenia

Management:

- Supportive treatment
- DISCONTINUE Abacavir immediately and never use it again

Didanosine (ddI; Videx[®])

Dose:

< 3 months:

50 mg/m²/dose

3 months to < 13 yrs:

90 - 120 mg/m²/dose

≥ 13 yrs or > 60 kg:

200 mg/m²/dose

Frequency:

12 hourly

Formulation:

Suspension - 10 mg/ml

(stable for 30 days; requires refrigeration)

Tablets - 25 mg, 50 mg, 100 mg & 150 mg (buffered)

Comments:

- Do not administer with food - give 1 hour before or 2 hours after meals
- Suspension must be reconstituted with antacid
- If 2½ tablets are required per dose this is best achieved by giving 2 tablets in the morning and 3 tablets at night

Side effects:

Common

Abdominal pain

Diarrhoea

Nausea & vomiting

NB: Each dose must include
at least TWO tablets to ensure
adequate intake of buffer per dose

Rarer

Pancreatitis

Peripheral neuropathy

Lactic acidosis (exclude other causes of lactic acidosis such as hypovolaemia or septic shock)

Note:

The dose calculations in the above table have opted for simplicity for the caregiver (i.e. only 25 mg tablets used), recognizing that this increases the pill burden for the child. If this is problematic adjust the tablet strengths accordingly, ensuring that each dose includes at least 2 tablets.

Lamivudine (3TC[®])

Dose:

4 mg/kg/dose

Frequency:

12 hourly

Formulation:

Syrup - 10 mg/ml

Tablets - 150 mg

Comments:

- Can be administered with food
- If $\frac{3}{4}$ tablet is required per dose this is best achieved by giving $\frac{1}{2}$ tablet in the morning and 1 tablet at night

Side effects:*Common*

Headache
Fatigue
Nausea & diarrhoea
Skin rash
Abdominal pain

Rarer

Pancreatitis
Peripheral neuropathy
↓ WCC
↑ Liver enzymes

Stavudine (D4T; Zerit[®])

Dose:

1 mg/kg/dose

Adolescents:

< 40 kg 20 mg bd

< 60 kg 30 mg bd

Frequency:

12 hourly

Formulation:

Suspension - 1 mg/ml

(requires refrigeration)

Capsules - 20 mg, 30 mg & 40 mg

Comments:

- Can administer with food
- Do not combine with AZT
- Combination with ddI has ↑ rate of toxicity
- To reconstitute, dissolve 20 mg capsule in 20 ml water giving a concentration of 1 mg/ml (if only using ½ capsule – discard remaining half)

Side effects:*Common*

Headache

GIT disturbance

Skin rash

Rarer

Pancreatitis

Peripheral neuropathy

↑ Liver enzymes

Lactic acidosis (exclude other causes of lactic acidosis such as hypovolaemia or septic shock)

Zidovudine (AZT; Retrovir[®])

Dose:

180 - 240 mg/m²/dose

Frequency:

12 hourly

Formulation:

Syrup - 10 mg/ml

Capsules - 100 mg

Tablets - 300 mg

Comments:

- Better tolerated with food
- Do not give with D4T
- Do monthly FBC for first 3 months after starting AZT
- If 1½ capsules are required per dose this is best achieved by giving 1 capsule in the morning and 2 capsules at night

Side effects:*Common*

Headache

Anaemia

↓ granulocytes

Rarer

Myopathy

Efavirenz (Stocrin®)

Dose:

See Simplified Dosing in Resource Poor Settings table (Appendix VIII)

Frequency:

Daily

Formulation:

Capsules - 50 mg & 200 mg

Tablets - 600 mg

Comments:

- Not suitable for children < 10kg or < 3 years of age
- Give at night to avoid CNS side-effects
- Preferably take on empty stomach

Side effects:*Common*

Skin rash

CNS – drowsiness, insomnia, abnormal dreams, confusion, poor concentration, hallucinations, amnesia

Rarer

↑ Liver enzymes

Nevirapine (Viramune®)

Dose:

160 - 200 mg/m²/dose

Frequency:

Daily for 14 days

THEN

12 hourly

Formulation:

Syrup - 10 mg/ml

Tablets - 200 mg

NVP for PMTCT by Age	Daily dose	
	mg	ml
Birth to 6 wks (< 2.5 kg)	10 mg	1 ml
Birth - 6 wks (> 2.5 kg)	15 mg	1.5 ml
6 wks - 6 months	20 mg	2 ml
6 - 9 months	30 mg	3 ml
9 months to end of breast feeding	40 mg	4 ml

Comments:

- Can administer with food
- Skin rash can occur within first 6 weeks – do not increase dose until rash resolves
- Stop treatment if ALT \uparrow

Side effects:

Common

Skin rash (including Stevens
Johnson & Toxic Epidermal
Necrolysis)
Sedation
Diarrhoea

Rarer

Liver toxicity (\uparrow liver
enzymes, RUQ pain etc)
Hypersensitivity reaction
(rash, fever, oral sores,
conjunctivitis & facial
oedema)

NVP for ART by Weight (kg)	Single dose by weight (kg)		
	mg	ml	Tablets
< 3	CONSULT LOCAL REFERRAL CENTRE		
3 - 3.9	50 mg	5 ml	-
4 - 4.9	50 mg	5 ml	-
5 - 5.9	50 mg	5 ml	-
6 - 6.9	80 mg	8 ml	-
7 - 7.9	80 mg	8 ml	-
8 - 8.9	80 mg	8 ml	-
9 - 9.9	80 mg	8 ml	-
10 - 10.9	100 mg	10 ml	½ tablet
11 - 11.9	100 mg	10 ml	½ tablet
12 - 13.9	100 mg	10 ml	½ tablet
14 - 16.9	150 mg	15 ml	¾ tablet*
17 - 19.9	150 mg	16 ml	¾ tablet*
20 - 24.9	150 mg	17 ml	¾ tablet*
25 - 29.9	200 mg	20 ml	1 tablet
30 - 34.9	200 mg	20 ml	1 tablet
35 - 39.9	200 mg	20 ml	1 tablet
> 40	200 mg	20 ml	1 tablet

* best achieved by giving: 1 tablet in the morning
and ½ tablet at night

Hepatotoxicity

Hepatotoxicity occurs mainly in the first 8 weeks after starting nevirapine

The patient may present with nausea, vomiting, right upper quadrant tenderness, and jaundice if severe.

Management:

- Grade the level of toxicity based on the LFT and bilirubin (see pg 26)
- Antiretrovirals should be stopped if the toxicity is grade 3 or 4
- If Grade 1 or 2 toxicity occurs clinically assess patient and repeat liver function tests within a week, or consult local referral centre
- Skin rash associated with nevirapine toxicity may occur in association with liver dysfunction - always check liver function tests if skin rash occurs

Lopinavir/Ritonavir (Kaletra[®] / Aluvia[®])

Dose:

230 - 400 mg LPV/m²/dose

Frequency:

12 hourly

Formulation:

Syrup (Kaletra[®])

- 80 mg LPV & 20 mg RTV/ml
(requires refrigeration)

Tablets (Aluvia[®])

- 200 mg LPV / 50 mg RTV

Comments:

- Administer Kaletra[®] with food (high fat meal increases absorption)
- In regimen with ddI give Kaletra[®] 1 hour after or 2 hours before ddI
- Aluvia[®] may be given with or without food
- If the required dose is 1½ tablets this is best achieved by giving 1 tablet in the morning and 2 tablets at night

Side effects:*Common*

Diarrhoea

Nausea & vomiting

Rarer

↑ Cholesterol

↑ Triglycerides

Diabetes & hyperglycaemia

Additional Ritonavir for children on TB treatment (with Rifampicin)

Dose:

Prescribing **additional Ritonavir**

to give a 1:1 ratio (mg) for Lopinavir/Ritonavir is currently recommended
(NOT double-dosing of Kaletra[®] as previously recommended)

N.B. The increased dose of Ritonavir is required to counteract the enhanced metabolism of Kaletra[®] due to induction of liver enzymes by rifampicin (TB treatment)

Frequency:

12 hourly

Formulation:

Syrup - 80 mg/ml

(at room temperature for
30 days only - otherwise refrigerate)

Capsules - 100 mg

Comments:

- On completion of TB treatment, continue with additional Ritonavir for two weeks after Rifampicin has been discontinued, and then discontinue Ritonavir
- If the required dose is 1½ capsules or 2½ capsules this is best achieved by giving 1 capsule in the morning and 2 capsules at night, or 2 capsules in the morning and 3 capsules at night respectively

Simple alternative method for calculating additional dose of Ritonavir:

When using syrup, the additional dose of Ritonavir is 0.75 times the volume of the Kaletra dose
e.g. if the Kaletra dose is 2 ml 12 hourly,
then the additional Ritonavir dose will be $0.75 \times 2 = 1.5$ ml 12 hourly

SIMPLIFIED PAEDIATRIC DRUG DOSING FOR RESOURCE POOR SETTINGS: First Line

Weight (kg)	ABACAVIR	D4T	3TC	EFAVIRENZ	LPV/r (Kaletra®/Aluvia®)		ADDITIONAL RITONAVIR	Bactrim (PCP Proph)		Multivitamins	
	8 mg/kg/dose twice daily Syrup 20 mg/ml Tablets 300 mg	1 mg/kg/dose twice daily Suspension 1 mg/ml Capsules 15, 20, 30 mg	4 mg/kg/dose twice daily Syrup 10 mg/ml Tablets 150 mg	Once daily Capsules 50, 200 mg Tablets 50, 200, 600 mg	300/75 mg/m ² /dose twice daily Syrup (Kaletra®) 80/20 mg/ml Tablets (Aluvia®) 200/50 mg		Added to LPV/r while on Rifampicin twice daily Syrup 80 mg/ml	Daily Syrup 40/200 mg/5ml Tablets 80/400 mg		Daily Syrup, or Tablets	
< 3	CONSULT LOCAL REFERRAL CENTRE							2.5 ml		2.5 ml	
3 – 3.9	3 ml	6 ml	3 ml		1 ml		1 ml		2.5 ml	2.5 ml	
4 – 4.9	3 ml	6 ml	3 ml		1.5 ml		1.2 ml		2.5 ml	2.5 ml	
5 – 5.9	3 ml	7.5 ml	3 ml		1.5 ml		1.2 ml		5 ml	½ tab	2.5 ml
6 – 6.9	3 ml	7.5 ml	4 ml		1.5 ml		1.2 ml		5 ml	½ tab	2.5 ml
7 – 7.9	4 ml	10 ml	4 ml		1.5 ml		1.2 ml		5 ml	½ tab	2.5 ml
8 – 8.9	4 ml	10 ml	4 ml		1.5 ml		1.2 ml		5 ml	½ tab	2.5 ml
9 – 9.9	4 ml	10 ml	4 ml		1.5 ml		1.2 ml		5 ml	½ tab	2.5 ml
10 – 10.9	6 ml	15 ml	6 ml	200 mg	2 ml		1.5 ml		5 ml	½ tab	5 ml
11 – 11.9	6 ml	15 ml	6 ml	200 mg	2 ml		1.5 ml		5 ml	½ tab	5 ml
12 – 13.9	6 ml	15 ml	6 ml	200 mg	2 ml		1.5 ml		5 ml	½ tab	5 ml
14 – 16.9	7 ml or ½ tab	20 mg	7.5 ml or ½ tablet	200 mg + 50 mg	2.5 ml		2 ml		10 ml	1 tab	5 ml
17 – 19.9	8 ml or ½ tab	20 mg	7.5 ml or ½ tablet	200 mg + 50 mg	2.5 ml		2 ml		10 ml	1 tab	5 ml
20 – 24.9	10 ml or 1 tab am ½ tab pm	20 mg am 30 mg pm	1 tablet am ½ tablet pm	200 mg + 2 x 50 mg	3 ml		2.5 ml		10 ml	1 tab	5 ml
25 – 29.9	1 tablet	30 mg	1 tablet	200 mg + 3 x 50 mg	3.5 ml	2 tab am 1 tab pm	3 ml		10 ml	1 tab	5 ml
30 – 34.9	1 tablet	30 mg	1 tablet	2 x 200 mg	4 ml	2 tab am 1 tab pm	3 ml		2 tablets		1 tablet
35 – 39.9	1 tablet	30 mg	1 tablet	2 x 200 mg	5 ml	2 tab	4 ml		2 tablets		1 tablet
> 40	1 tablet	30 mg	1 tablet	600 mg	5 ml	2 tab	4 ml		2 tablets		1 tablet

SIMPLIFIED PAEDIATRIC DRUG DOSING FOR RESOURCE POOR SETTINGS: Second Line and TB Treatment

Weight (kg)	AZT	DDI	LPV/r (Kaletra®/Aluvia®)	ADDITIONAL RITONAVIR	Intensive TB treatment* (first 2 months) Daily	Maintenance TB Treatment* (last 4 months) Daily	Bactrim (PCP Proph) Daily	Multivitamins Daily		
	240 mg/m ² /dose twice daily Syrup 10 mg/ml Capsules 100 mg Tablets 300 mg	90 - 120 mg/m ² /dose twice daily Tablets 25, 50, 100 mg Capsules 250mg EC	300/75 mg/m ² /dose twice daily Syrup (Kaletra®) 80/20 mg/ml Tablets (Aluvia®) 200/50 mg	Added to LPV/r while on Rifampicin twice daily Syrup 80 mg/ml	RHZ 60/30/150 mg Rimcure Paed	RH 60/30 mg Rifanah Sachets	Syrup 40/200 mg/5ml Tablets 80/400 mg	Syrup, or Tablets		
< 3	CONSULT LOCAL REFERRAL CENTRE				½ tablet	½ tablet	2.5 ml	2.5 ml		
3 – 3.9	6 ml		1 ml	1ml	1 tablet	1 tablet	2.5 ml	2.5 ml		
4 – 4.9	6 ml		1.5 ml	1.2ml	1 tablet	1 tablet	2.5 ml	2.5 ml		
5 – 5.9	6 ml	2 x 25 mg	1.5 ml	1.2ml	1 tablet	1 tablet	5 ml	½ tab	2.5 ml	
6 – 6.9	9 ml	2 x 25 mg	1.5 ml	1.2ml	1½ tablets	1½ tablets	5 ml	½ tab	2.5 ml	
7 – 7.9	9 ml	2 x 25 mg	1.5 ml	1.2ml	1½ tablets	1½ tablets	5 ml	½ tab	2.5 ml	
8 – 8.9	9 ml	2 x 25 mg	2 ml	1.2ml	1½ tablets	1½ tablets	5 ml	½ tab	2.5 ml	
9 – 9.9	9 ml	2 x 25 mg	2 ml	1.2ml	2 tablets	2 tablets	5 ml	½ tab	2.5 ml	
10 – 10.9	12 ml	50 mg + 25 mg am 2 x 25 mg pm	2 ml	1.5ml	2 tablets	2 tablets	5 ml	½ tab	5 ml	
11 – 11.9	12 ml	50 mg + 25 mg	2 ml	1.5ml	2 tablets	2 tablets	5 ml	½ tab	5 ml	
12 – 13.9	12 ml	50 mg + 25 mg	2 ml	1.5ml	2½ tablets	2½ tablets	5 ml	½ tab	5 ml	
14 – 14.9	2 caps am 1 cap pm	2 x 50 mg am 50 mg + 25 mg pm	2.5 ml	2ml	2½ tablets	2½ tablets	10 ml	1 tab	5 ml	
15 – 16.9	2 caps am 1 cap pm	2 x 50 mg am 50 mg + 25 mg pm	2.5 ml	2ml	3 tablets	3 tablets	10 ml	1 tab	5 ml	
17 – 19.9	2 caps am 1 cap pm	2 x 50 mg	2.5 ml	2ml	3 tablets	3 tablets	10 ml	1 tab	5 ml	
20 – 24.9	2 capsules	100 mg + 25 mg or 250 mg EC	3 ml	2.5ml	4 tablets	4 tablets	10 ml	1 tab	5 ml	
25 – 29.9	1 tablet	100 mg + 25 mg or 250mg EC	3.5 ml	2 tab am 1 tab pm	3ml	5 tablets	5 tablets	10 ml	1 tab	5 ml
30 – 39.9	1 tablet	100 mg + 25 mg or 250mg EC	4 ml	2 tab am 1 tab pm	3ml	6 tablets	6 tablets	2 tablets	1 tab	
> 40	1 tablet	100 mg + 25 mg or 250mg EC	5 ml	2 tablets	4ml	Adult dose	Adult dose	2 tablets	1 tab	

*Adapted from Guidance for National Tuberculosis Programmes on the Management of Tuberculosis in Children, World Health Organization 2006 and South African National Tuberculosis Guidelines 2008 (draft)