Swaziland Paediatric HIV Guidelines

2010

Ministry of Health and Social Welfare

Foreword

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These guidelines are dedicated to the HIV-exposed and infected children of Swaziland with the hope of providing them the opportunity to live long, healthy, and productive lives. We would particularly like to acknowledge the families and caregivers of these children whose dedication, commitment, and perseverance makes successful care and treatment possible.

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Abbreviations

3TC	Lamivudine, Epivir
ABC	Abacavir, Ziagen
AFB	Acid Fast Bacillae
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine aminotransferase
ANC	Ante natal care
ART	Anti-Retroviral Therapy
ARV	Anti-RetroViral
AST	Aspartate Amino Transferase
AZT	Zidovudine, Retrovir
BAL	Broncho Alveolar Lavage
BCG	Bacille de Calmette et Guerin
BD	twice per day
BF	Breastfeeding
BSA	body surface area
CD4	Cluster of Differentiation 4
CDC	Center for Disease Control
CIHTC	Client Initiated HIV Testing and Counselling
cm	centimeter
CMV	Cytomegalovirus
CNS	Central Nervous System
CrAg	Cryptococcal Antigen
CrCl	Creatinine Clearance
CSF	cerebrospinal fluid
CT	computed tomography
CTX	Cotrimoxazole, Cozole, Bactrim
CXR	chest x-ray
d4T	stavudine, Zerit
DBS	Dried Blood Spot
ddI	didanosine, Videx
DHS	Demographic Health Survey
DIC	Disseminated Intravascular Coagulation
dl	Deciliter
DNA	Deoxyribonucleic Acid
DPT	Diphtery Pertussis Tetanus
E	Ethambutol
EAT	Early Antiretroviral Therapy
EBF	Exclusive Breastfeeding
EBV	Epstein Barr Virus
EFV	efavirenz, Sustiva
EID	Early Infant Diagnosis
ELISA	Enzyme-Linked Immunosorbent Assay
ERF	Exclusive Replacement Feeding
FBC	Full Blood Count
FDC	Fixed Dose Combination
FP	Family Planning
g	gram
H	INH - Isoniazid
H_2O	Water
Hb	Hemoglobin
HBV	Hepatitis B Virus
HCW	Health Care Worker
HIV	Human Immunodeficiency Virus
IV	intravenous
Kg	kilograms
KS	Kaposi Sarcoma
LFTs	Liver Function Tests
LGE	Lineal gingival erythema
LIP	Lymphoid Interstitial Pneumonitis
LP	lumbar puncture
LPV/r	lopinavir boosted with ritonavir
LTB	Laryngeotracheobronchitis
m^2	meters squared
MAC	Mycobacterium Avium Complex
MDR TB	Multiple Drug Resistant Tuberculosis
Mg	milligrams
ml	milliliter
mm^3	millimeters cubed
MOH	Ministry of Health
MRI	magnetic resonance imaging
MTCT	Mother To Child Transmission
MUAC	Mid Upper Arm Circumference
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NPA	Nasal Pharyngeal Aspirate
nPEP	non-occuptional post exposure prophylaxis
NRL	National Reference Laboratory
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NtRTI	Nucleotide Reverse Transcriptase Inhibitor
NVP	Nevirapine, Viramune
OD	once per day
OI	Opportunistic Infection
OVC	Orphaned and Vulnerable Children
PCP	Pneumocystis Jirovecii Pneumonia
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
PGL	Persistent Generalised Lymphadenopathy
PI	Protease Inhibitor
PIHTC	Provider Initiated HIV Testing and Counselling
PML	Progressive Multifocal Leukoencaephalopathy
PMTCT	Prevention of Mother To Child Transmission
PO	orally
PPD	Purified Protein Derivate
QID	four times a day
R	Rifampicin
RNA	Ribonucleic Acid
RTHC	Road To Health Card
SD	Standard deviation
SQV	Saquinavir
STI	Sexually Transmitted Infection
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
TDS	three times a day
TLC	Total Lymphocyte Count
TMP	Trimethoprim
TMP-SMX	Trimethoprim- Sulfamethoxazole
TST	Tuberculin Skin Testing

HSV	Herpes Simplex Virus
HTC	HIV Testing and Counselling
ICD	Immune Complex Dissociated
IM	Intramuscular
IMCI	Integrated Management of Childhood Illnesses
IMR	Infant Mortality Rate
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
IRIS	Immune reconstitution inflammatory syndrome
IU	International Units
UNAIDS	Joint United Nations Program on HIV/AIDS
UNICEF	United Nations Children's Fund
URTI	Upper Respiratory Tract Infection
VL	Viral Load
W/H	Weight for Height
WHO	World Health Organization
XDR TB	Extreme Drug Resistant Tuberculosis
ZDV	zidovudine, Retrovir (AZT)
Z-N	Ziehl Nielsen
Z	Pyrazinamide

Executive Summary

Many changes have occurred following new research in the field of paediatric HIV prevention, care and treatment necessitating revision of the *2006 Swaziland Paediatric HIV/AIDS Treatment Guidelines*. The present guidelines are part of Swaziland's commitment to achieve universal access to prevention, care and treatment of HIV infection in infants and children, and reflect changes in the 2010 WHO paediatric guidelines[1]. A summary of major changes from the previous guidelines and highlights of the new guidelines are detailed here.

Paediatric HIV Testing and Counselling

- Early Infant Diagnosis: All HIV-exposed infants should receive an initial DBS DNA PCR HIV test at the 6 week well-child visit.
  - For children less than 18m with an initial positive DNA PCR test, a repeat virologic test should be conducted with baseline ART initiation labs. Either viral load or a second DNA PCR is acceptable.
  - For children with an initial negative DNA PCR test, a repeat HIV test should be conducted 6-8w after cessation of breastfeeding.

- Window period: The window period for antibody-based rapid tests is now 2 months (instead of 3 months).

- Consent: The age of consent for HIV testing is 16 years, however premature adults (pregnant, accessing STI or family planning services, or sexually active) may give their own informed consent.

Care of HIV-Exposed Infants

- Breastfeeding: All infants should be exclusively breastfed for the first six months of life, with complimentary feeding thereafter. At 12 months, HIV infected children should continue to breastfeed as long as possible; healthy HIV-negative children should gradually stop breastfeeding if a nutritionally adequate and safe diet is available.

- Extended NVP Prophylaxis: All HIV exposed infants will receive extended NVP prophylaxis for at least 6 weeks postpartum. Breastfeeding infants will continue with NVP prophylaxis until 1 week after cessation of breastfeeding.

- INH Preventive Therapy: Infants with household TB contacts should be given isoniazid preventive therapy (IPT) for 6 months after active TB infection has been excluded.

- CTX Prophylaxis: As per previous guidelines, daily cotrimoxazole should be given to all exposed infants until HIV status is definitively negative.

- Visit schedules for exposed infants are now linked with the immunization schedule.

[1] World Health Organization. Antiretroviral therapy for HIV infection in infants and children: Towards universal access. Recommendations for a public health approach: 2010 revision.

Care of HIV-Infected Infants and Children

- ART Initiation Criteria: Emphasis is placed on early initiation of treatment.

Criteria for Initiating ART in Infants and Children		
	WHO Clinical Stage 1-2	**WHO Clinical Stage 3-4**
Under 24 months	Treat all	
2-14 years	CD4 guided 2-4.9 years: ≤25% 5 years and over: ≤350	Treat all

- Routine Laboratory Monitoring: Lab tests should not be a barrier to initiating treatment. Routine lab monitoring has been minimized based on evidence demonstrating equivalent outcomes with symptom-directed versus routine lab monitoring.

Visit	Minimum labs recommended
Baseline	CD4 and Hb DNA PCR or viral load if <18m
4w post-initiation	Hb (if on AZT)
Every 6m	CD4 Hb (if on AZT); Glucose, lipids (if on LPV/r)
Other laboratory tests should be conducted as directed by symptoms	

- First-line ART Regimens: New recommendations focus on use of fixed-dose combination formulations. Children under 2 years who receive NVP prophylaxis should be initiated on LPV/r due to the high likelihood of NVP resistance. The new recommendations for children 12 years and older reflect changes in the Swaziland Adult Guidelines.

Recommended First-Line ART Regimens				
Under 2 years		**2 - 11.9 years**	**12 years and older**	
NVP-exposed	*NOT* NVP-exposed	(Regardless of NVP exposure)	<40kg	≥40kg
AZT–3TC–LPV/r	AZT–3TC–NVP	AZT–3TC–NVP	AZT–3TC–NVP	TDF–3TC–EFV
Once initiated, children should continue on their initial regimen for life unless a switch is indicated (e.g. toxicity, development of TB, simplification of regimen, or treatment failure)				

- Special Considerations: Given multiple co-morbidities associated with HIV infection, the potential for drug-drug interactions, and the complex psychosocial circumstances of many families, these guidelines provide detailed alternative options and recommendations for specific circumstances.

- Phasing-Out of d4T: Due to its many long-term side effects, any child on d4T who does not have known toxicity to AZT should be switched to AZT as long as the Hb>10.

- Retention on First-Line Regimens: These guidelines emphasize the development of structures to provide ongoing support and monitoring of adherence with the goal of retaining children on first-line regimens as long as possible. Treatment failure must be confirmed based on new specific clinical, immunologic, virologic, and psychosocial criteria detailed in Chapter 4. A switch to second line should only be considered when a strong plan for treatment success has been designed by a multidisciplinary team in conjunction with the child's family/caregivers.

- Second-Line ART Regimens: Recommendations for second-line regimens promote LPV/r as the backbone (similar to previous guidelines) for children who have been on NNRTI-based first-line regimens. With the change to encourage fixed-dose combinations to promote adherence, ABC-3TC (for children under 12 years) or TDF-3TC (for children over 12 years) are the recommended NRTIs. ddI is no longer part of the standard second-line regimen, although children currently on ddI and doing well may continue. An NNRTI will likely need to be used as second-line for children initiated on LPV/r who develop treatment failure.

Management of Common Illnesses and Opportunistic Infections

- Decreasing morbidity and mortality: In an effort to decrease morbidity and mortality, early and aggressive diagnosis and treatment of illness is emphasized. A standardized approach to management has been added to these guidelines.

Nutrition in HIV

- Nutritional monitoring: Nutritional status by weight-for-height and/or MUAC should be evaluated at every visit. Tools for assessment and suggestions for interventions are provided in these guidelines.

- Infant feeding: New infant feeding recommendations are detailed in this chapter and summarized in the exposed infant section above.

TB/HIV Co-Infection

- TB screening: Due to the high prevalence of TB in Swaziland, these guidelines emphasize screening for TB at each pre-ART or ART follow-up visit. Aggressive evaluation is indicated for those who screen positive.

- Timing of ART initiation: Recent studies demonstrate decreased morbidity and mortality with early initiation of ART following TB treatment. ART should therefore be initiated 2-8 weeks after initiation of TB treatment irrespective of CD4.

- ART regimens for children co-infected with TB: In children, options for effective ART regimens are limited due to drug-drug interactions with rifampicin. The guideline development team therefore chose regimens that facilitate adherence and while minimizing medication interactions. Detailed recommendations for recommended ART regimen following TB treatment are outlined in Chapter 7.

HIV/TB Co-treatment ART Regimens for Children who are treatment naïve or on any first-line ART Regimen	
Age < 3 years	**Age > 3 years**
AZT – 3TC – NVP	AZT – 3TC – EFV

- No lead-in dosing: If patient is on TB therapy, NVP should be initiated at twice daily dosing. Due to enzyme induction by rifampicin, lead in dosing is not indicated and will increase the risk of developing NVP resistance.

- Isoniazid Preventive Therapy (IPT): All HIV-infected children without active TB should be initiated on IPT. If a child is about to initiate ART, IPT should be delayed until 6 months after initiation of ART. IPT should be repeated at minimum every 3 years. If known close TB contact then repeat IPT earlier after ruling out active TB.

Care of HIV-infected Adolescents

- Addressing adolescent-specific issues: With more children living longer on ART, Swaziland is experiencing an increase in the prevalence of HIV in the adolescent population. The need to advocate for provision of adolescent-friendly services including adherence strategies, sexuality counselling, and peer support services is emphasized.

Psychosocial Care and Counselling

- Age appropriate counselling: The importance of age-appropriate counselling is highlighted and strategies for counselling children of various ages and developmental stages are provided.

- Disclosure: More often than not, children are aware of their status well before disclosure takes place. These guidelines provide information on the benefits of disclosure and strategies to assist HCW in disclosing to children and caregivers.

Monitoring and Evaluation

- Paediatric-specific indicators have been incorporated in the national PMTCT and ART monitoring and evaluation system emphasizing uptake of PMTCT interventions, early infant diagnosis, linkage to care and treatment, and retention on ART.

Chapter 1 Introduction

1.1 Progress since 2006

In Swaziland, great strides have been made since the release of the 2006 *Swaziland Paediatric HIV/AIDS Treatment Guidelines*. Uptake of more efficacious PMTCT regimens is leading to a decrease in new infant infections. DNA PCR HIV testing has become available throughout the country allowing for early infant diagnosis and antiretroviral therapy (ART) initiation. Paediatric fixed-dose combination tablets have dramatically improved the treatment options available for children. Consequently, HIV-related mortality is decreasing. These improvements in paediatric diagnosis, care, treatment and survival lead to an estimated increase in the overall number of HIV-infected children who will need ongoing care and treatment services (Table 1). These estimates clearly show the need for Swaziland to urgently increase access to treatment and care services for HIV-exposed and infected children.

Table 1. Swaziland Paediatric HIV and AIDS Estimates[2]

Swaziland Paediatric HIV Estimates	2010	2015
HIV population: Children 0-14 years	14,613	17,213
Annual AIDS-related deaths: children 0-14 years	1,016	462
Children (0-14 years) in need of ART	9,827	14,880
Mothers needing PMTCT	9,260	8,421
Total number of new infant (<12m) infections	1,956	1,623

1.2 Prevention of New Infant Infections

Interventions must begin with an accelerated effort to prevent new paediatric infections. Mother-to-child-transmission of HIV (MTCT) during pregnancy, labour and delivery, and during the breastfeeding period is responsible for over 90% of new paediatric HIV infection. Given the high HIV prevalence of 42% among pregnant women[3], and the annual births of 33000[4], approximately 13800 infants are exposed to HIV annually. Without any intervention, as many as 5500 (40%) of these infants could become infected. As of 2009, 75% of HIV-infected pregnant women are receiving ARV prophylaxis to prevent MTCT resulting in an infant prevalence of about 11%[5]. New and aggressive PMTCT strategies can reduce transmission to less than 5%. Linkages between ANC, maternity, and child welfare clinics, and an integrated approach to care, will be crucial in meeting this prevention goal.

[2] Spectrum data (UNAIDS, July 2010)
[3] Sentinel Surveillance among ANC women, (2008)
[4] MOH, Strategic Information Department
[5] MOH, Strategic Information Department

1.3 The Need for Early Diagnosis and Treatment

The under 5 mortality in Swaziland is high at 120 deaths per 1000 live births[6], 47% of which are attributed to HIV[7]. HIV is rapidly progressing in 80% of infected infants. Consequently, without early care and ART initiation, more than one-third of HIV-infected children will die within one year and over a half by two years of age (Table 2). These sobering statistics emphasize the need to ensure that HIV-infected children receive ART early.

Table 2. Mortality for untreated HIV infected children[8]

Mortality for untreated HIV infected children	
At 1 year	35.2%
At 2 year	52.5%
At 5 year	66 – 75%
At 10 years	85%

In 2007, Swaziland introduced early infant diagnosis using DNA PCR testing on dry blood spot samples allowing for diagnosis of HIV infection as early as six weeks of age. Over the last three years, the National Reference Laboratory has developed the capacity to run this test in Swaziland. These interventions have resulted in the testing of about 10000 infants annually. The CHER study in South Africa has demonstrated that early ART reduces HIV related mortality by as much as 75%[9]. Given the rapid expansion of early infant diagnosis, the country has opportunities to initiate HIV infected children on ART and reduce most of the deaths that would have otherwise occurred before the child was two years of age.

Access to life saving ARVs has improved greatly in Swaziland over the last few years but there remains a gap in children accessing ART care. According to UNICEF, only 46% of HIV infected children in need of ART are receiving it. While this is an improvement from 42% in 2007, more can be done to increase the number of children on ART. Communities need to be sensitized of the need for early intervention. Decentralization of paediatric ART services in line with the national ART decentralization plan will make care and treatment more accessible. Training of HCW on paediatric diagnosis, care and treatment as well as paediatric phlebotomy, will be a necessary component of this strategy. Finally, procurement and distribution of paediatric FDCs will help to simplify treatment and facilitate adherence for children, caregivers, and health care workers. With these interventions, Swaziland can meet the challenge of ensuring that all HIV-infected children in need receive quality care and ART.

[6] Swaziland demographic Health survey (DHS), 2007
[7] Child Health Epidemiological reference Group, CHERG, 2004
[8] Newell et al, 2004 and Spira et al, 1999
[9] Violari, et. al. CHER Study. 2008.

1.4 A Family-Centred Approach

In Swaziland there are approximately 15,000 children are living with HIV and 56,000 AIDS orphans[10]. Even HIV-negative infants born to HIV-infected mothers have a 2- to 5-fold increased risk of mortality as a direct consequence of the mother's HIV infection. A family-centred approach to care is therefore crucial at the individual health care workers (HCW) level as well as at facility and health system levels. Integrated care models should be implemented to address the needs of all family members, including testing all family members, enrolling them into care, and designing community support structures to decrease stigma and facilitate access to services. This approach will increase enrolment, improve patient follow up, decrease infection rates, and ultimately decrease mortality and morbidity.

1.5 What to Expect in the Revised Guidelines

The guidelines have ten well structured chapters with content that address prevention, diagnosis, care, and treatment including:

1. Alignment with the PMTCT guidelines: HIV negative but exposed children will be provided with extended ARV prophylaxis throughout the breastfeeding period to prevent HIV infection from breast milk.
2. Alignment with the HTC guidelines: Provider-initiated HTC is emphasized and issues of paediatric counselling and consent are expanded upon.
3. A description of the package of comprehensive care services that should be offered to HIV exposed and infected children.
4. New evidence in the management of HIV infected children: All HIV infected children under 2 years of age will be initiated on ART irrespective of clinical or immunologic stage. A protease inhibitor-based first line regimen is now recommended for children less under two years of age who were exposed to nevirapine.
5. Criteria for evaluating treatment failure and switching to second line.
6. Guidance on management of common opportunistic infections
7. Tools for nutritional assessment and interventions to prevent malnutrition
8. Expanded information on the management of TB/HIV co-infected children and recommendations for isoniazid preventive therapy (IPT).
9. Guidance on adolescent-specific issues including reproductive health needs.
10. Recommendations for disclosing to children and addressing psychosocial challenges.

[10] UNAIDS 2008 Report

Chapter 2 Paediatric HIV Testing and Counselling

2.1 Who to Test

In Swaziland in 2008, 42% of women presenting to ANC clinics were HIV infected[11] resulting in the birth of about 13,800 exposed infants[12]. The 2007 Demographic Health Survey (DHS) revealed that about 4% of children aged 2-14 years are HIV positive. Further, with early sexual debut, adolescents are also at high risk of HIV infection. As early ART has been shown to save lives, it is imperative that all exposed infants and children are tested.

ALL infants and children need their HIV status to be known including
A. Exposed infants and children less than 18 months
B. Infants, children, or adolescents with clinical suspicion of HIV
C. Infants, children, and adolescents coming for routine care services

A. EXPOSED INFANTS AND CHILDREN LESS THAN 18 MONTHS

The vast majority of HIV infections in children are via mother-to-child-transmission (MTCT). These children are at highest risk of disease progression and death. Children carry their mothers' antibodies up to 18 months of age, and therefore the exposure status of an infant can be established by offering HIV Testing and Counselling (HTC) to either the mother or to the child.

Exposed infants or children <18 months are those who:

- Are born to HIV+ mothers (usually indicated on her pink ANC card)[13]
- Have a positive rapid antibody test

A positive rapid test in either the mother or the infant indicates that the infant has been exposed to HIV and should receive a DNA PCR test.

B. INFANTS, CHILDREN, AND ADOLESCENTS WITH CLINICAL SUSPICION OF HIV REGARDLESS OF HIV EXPOSURE

HCWs must always maintain a high level of clinical suspicion for HIV infection, regardless of exposure status. In a child less than 18 months, a presumptive diagnosis can be made on clinical ground alone per WHO criteria in Table 3 below.

[11] 2008 National Sentinel Survey
[12] Annual births 33,000; UNICEF 2007
[13] Mothers who tested HIV-negative during pregnancy may seroconvert so must be retested postpartum per PMTCT guidelines to confirm the exposure status of the infant.

Table 3. Presumptive diagnosis of HIV in infants and children under 18 months

A presumptive diagnosis of severe HIV disease should be made if:	
1. The child is confirmed as being HIV antibody-positive **AND**	2a. The infant is symptomatic with **two** or more of the following: ▪ oral thrush ▪ severe pneumonia ▪ severe sepsis **OR** 2b. Diagnosis of any AIDS-indicator condition(s)[a] can be made
Other things that support the diagnosis of severe HIV disease in an HIV-seropositive infant include: ▪ Recent HIV-related maternal death or advanced maternal HIV disease ▪ Child's %CD4+ < 20%	
Children meeting these criteria should immediately be referred for ART and the diagnosis of HIV infection should be confirmed as soon as possible with DNA PCR testing.	

[a] AIDS indicator conditions include some but not all HIV paediatric clinical stage 4 conditions such as Pneumocystis pneumonia, cryptococcal meningitis, severe wasting or severe malnutrition, Kaposi sarcoma, extrapulmonary tuberculosis.

Even if a mother was negative at the time of birth or a child has previously tested negative, that child could become infected later. Recurrent sick visits to the health facility should raise concern for HIV infection. Annex 1 describes the clinical signs and symptoms that should raise greatest concern for HIV infection. These children should be tested without delay.

Provide HTC for children with recurrent sick visits to the health facility.

C. ANY INFANT, CHILD, OR ADOLESCENT COMING FOR ROUTINE OR CURATIVE CARE SERVICES

Opportunities for HIV diagnosis and prevention counselling should not be missed. Healthcare providers should therefore routinely offer HTC to all infants, children, and adolescents presenting for any healthcare service. Further, children who have been sexually abused or potentially exposed to HIV via blood or potentially contaminated instruments should be tested.

2.2 Where to Test

Paediatric HIV testing should be conducted in all settings and entry points where adult testing is offered including stand-alone testing units, home based HTC and outreach settings. It should also be offered in paediatric-specific settings such as child welfare, paediatric OPD, and paediatric wards.

2.3 Consent, Confidentiality, and Counselling

The guiding principle healthcare workers should use in providing HTC to children is based on the UN Convention on the Rights of the Child which states that, "the best interests of the child shall be a primary consideration" in all actions concerning children. HIV testing and counselling (HTC) should be routinely offered by healthcare workers (Provider Initiated HTC - PIHTC) and may also be requested by the client or the client's guardian (Client Initiated HTC - CIHTC). The healthcare provider should always exercise professional judgment regarding the caregiver's intent for testing and the child's readiness to receive and accept the results of his/her HIV test.

The best interest of the child should be the primary consideration in HTC.

HTC must respect the WHO/UNAIDS "3 Cs" principle of obtaining verbal informed **consent**, ensuring **confidentiality** of the process and result, and providing **counselling** and support to *both* children and their caregivers. For more detailed information, refer to the *Swaziland National Guidelines on HIV Testing and Counselling*.

A. CONSENT

Age of Consent: Anyone age 16 years or above is able to give full informed consent[14]. In special circumstances, described below, children under age 16 may be able to give consent.

Who Can Provide Informed Consent: For children under the age of 16, parents, guardians, caregivers, HCWs, or social workers may provide informed consent for HTC[15]. The process of obtaining consent for HIV testing should be the same as for other medical procedures and diagnostic tests. In special circumstances, children may provide their own informed consent.

Box 1. Consent for Pediatric HTC

Age of consent is 16 years

Children considered premature adults may also give their own consent

Parents, guardians, caregivers, health care workers, or social workers may give consent for a child under 16.

Special Considerations for Consenting Children Under 16 Years:

- Premature adults – Children under the age of 16 may consent for HIV testing if they are pregnant, being treated for a sexually transmitted infection, accessing family planning services, or are sexually active.

[14] Girls' and Women's Protection Act (1920)
[15] Section 2.1.7.3 of the National Multisectoral HIV and AIDS Policy (2006)

- Absence of caregiver – Frequently, adolescents present to health care or testing facilities on their own or as the primary caregiver for a younger sibling. In situations where a parent, guardian or caregiver is not available, adolescents can identify a guardian, caregiver, HCW, or social worker to consent on their behalf. The process of obtaining consent for HIV testing should follow the same procedure as for other medical procedures and diagnostic tests, always keeping in mind the best interest of the child.

- Orphaned, Abandoned, and Vulnerable Children - Orphaned, abandoned, and abused children should be provided special attention, as they are at risk for discrimination, exploitation, and decreased access to health care. Healthcare workers should ensure that the child's caregiver is requesting or agreeing to HIV testing and counselling with the purpose of providing appropriate ongoing care and support for the child, regardless of the test outcome. Orphanage caregivers may give consent to testing, care, and treatment.

Advocacy for the development of legislation stipulating the age and circumstances under which minors can consent to medical procedures, including HIV testing, care, and treatment, is ongoing and will facilitate more timely interventions, including HTC.

B. CONFIDENTIALITY

Older children are often acutely aware of the social repercussions of an HIV diagnosis. They should be reassured of the confidentiality of the test result and supported in sharing the result only with those they trust.

C. COUNSELLING

Children should be counselled according to their level of development and maturity using age-appropriate language. Counselling dynamics may be significantly different in situations where a child is being counselled *with* a guardian, versus being counselled alone. HCWs need to be sensitive to these differences and address both the child's *and* the guardian's needs appropriately. For guardians, information provided should follow the *Swaziland National Guidelines on HIV Testing and Counselling* and include the benefits and potential risks of testing, meaning of results, assistance with disclosure, and referral to follow-up and support services. For children, every attempt should be made to explain to the child what is happening and to obtain her/his agreement to testing, care, and/or treatment. See Annex 2 for age-specific counselling considerations and guidance.

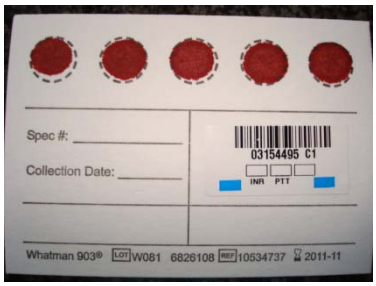
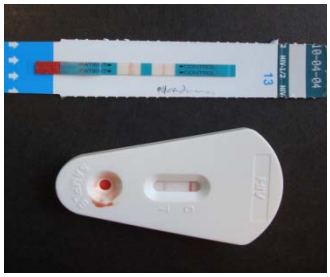
Children should be counselled according to their level of development and maturity using age-appropriate language.

2.4 When to Test and Which Test to Use

Test all HIV exposed infants at 6 weeks of age, during the 1st immunization visit, using DBS DNA PCR.

Exposed infants should be tested for HIV as early as six weeks of age. Because maternal antibodies may persist in a child until 18 months of age, virologic tests (DNA PCR) must be used to determine HIV status in children less than 18 months. 96% of infants lose maternal antibodies by 12 months of age, allowing for rapid testing to be used to rule-out HIV infection between 12 and 18 months, but DNA PCR must be used to confirm positive HIV status in this age group. Rapid antibody tests are used to confirm HIV status in children 18 months or older. Box 2 illustrates the type of test by age group. Algorithms detailing the testing pathways and clinical decision-making for each age group can be found in Annex 3.

Box 2. Diagnostic HIV Test by Child's Age

HIV Test by Child's Age		
6 weeks to 12 months	**12-18 months**	**18 months or older**
DNA PCR using Dry Blood Spot (DBS)  (Virology)	• Rapid Test "A" • If positive, confirm with DNA PCR using Dry Blood Spot (DBS)	Serial Rapid Tests using Rapid Test "A" then Rapid Test "B"  (Antibody)

2.5 Interpretation of HIV Test Results & Timing of Repeat Testing

It is strongly recommended that test results from virologic testing in infants be returned to the clinic and child/mother/caregiver as soon as possible, but at the very latest within four weeks of specimen collection. This allows for most results to be given at the 10 week immunization visit.

A. POSITIVE RESULT

For children less than 18 months of age a positive DNA PCR test should be considered diagnostic of HIV. Positive test results should be fast-tracked to the mother–baby pair. These children should be immediately referred to initiate ART without delay.

Children with a positive DNA PCR test should be immediately referred to initiate ART.

At the time baseline labs are drawn, a second specimen should be collected to confirm the initial positive test result using either viral load or DNA PCR. Immediate initiation of ART saves lives and commencement of ART should not be delayed while awaiting results of the confirmatory test. Confirmatory tests are unreliable once ART has been initiated as suppression of viral replication and antibody response may lead to falsely negative results.

A repeat virologic test should be conducted with baseline labs. ART initiation should not be delayed while awaiting results of the confirmatory test.

Serial positive rapid tests in children over 18 months are considered diagnostic of HIV infection.

B. NEGATIVE RESULT

An initial negative DNA PCR test should be confirmed 6 weeks after breastfeeding cessation to ensure that the child has not seroconverted during the period of breastfeeding exposure. All children who had an initial negative rapid test or negative DNA PCR should have a final rapid test conducted at 18 months to confirm negative status.

C. EQUIVOCAL OR INSUFFICIENT RESULT

Equivocal - DNA PCR test result meaning that the HIV status could not be determined. The test should be repeated immediately.

Insufficient – The DBS specimen was inadequate quantity or quality to process. The test should be repeated immediately.

Table 4. Interpretation of HIV test results

INTERPRETATION OF HIV TEST RESULTS			
Virologic DNA PCR Test			
Result	**Last Exposure**	**Interpretation**	**Action**
POSITIVE	N/A	Child is HIV infected	Refer for ART initiation; confirm with 2nd virologic test
NEGATIVE	Stopped BF at least 6 weeks before test	Child is HIV negative	Confirmatory rapid test at 18 months
	BF within 6 weeks of test	Child is still exposed	Repeat HIV test 6 weeks after BF cessation
EQUIVOCAL	N/A	Unable to determine status	Repeat DNA PCR test immediately
Serologic Rapid Antibody Test			
Result	**Last Exposure**	**Interpretation**	**Action**
POSITIVE	N/A	Younger than 18 months: Child is HIV exposed	Do DNA PCR to determine status
		Older than 18 months: Child is HIV infected	Refer for HIV care and treatment
NEGATIVE	Stopped BF at least 2 months before test	Child is HIV negative	
	BF within 2 months of test	Child is still exposed	Repeat rapid test 2 months after BF cessation
INCONCLUSIVE (1st POS, 2nd NEG)		Unable to determine status	Send blood sample to NRL for tie-breaker

D. VIRAL LOAD RESULT

Viral load may be used as a confirmatory test for children less than 18 months who have an initial DNA PCR positive result. Viral loads are reported as quantitative results. **Any detectable viral load is confirmation of HIV infection.** An undetectable viral load means that either no virus is present or the amount of virus is below the detectable level of the test. An undetectable viral load after a positive DNA PCR result is considered discordant, and a repeat DNA PCR should be conducted.

E. INCONCLUSIVE RESULTS

DNA PCR or rapid test whereby the initial test was positive and the confirmatory test was negative. A tie-breaker test should be conducted as soon as possible. For children less than 18 months, a DNA PCR test should be repeated. For children 18 months or older, a blood sample should be sent to the National Reference Laboratory (NRL) for the tie-breaker test.

2.6 Documentation

HIV testing and results should be documented in the patient's personal health record as well as in HTC and Child Welfare registers. As with other health conditions, care must be taken to record the results in a clear, yet confidential manner. To ensure consistency of reporting, "R" = Reactive (positive) and "NR" = Non-Reactive (negative). Other results (discordant, equivocal, or insufficient) are rare and should be documented in full with an explanation of the follow-up testing plan.

Results should be recorded confidentially:

Date _____: "HTC (or DNA PCR) done – Result R or NR"

Chapter 3 Care of the Exposed Infant

3.1 Importance of Close Follow-Up

Any infant who is born to an HIV-positive mother or tests positive for HIV antibodies before 18 months of age is considered to be HIV-exposed. HIV-exposed but uninfected infants have a higher morbidity and mortality than HIV-unexposed infants due to many factors including feeding choice and maternal health. HIV-infected children without any intervention have a more rapid disease progression compared to adults, with up to 35% mortality by 12 months of age. This high rate of early mortality is in large part due to malnutrition and more frequent respiratory and gastrointestinal tract infections that occur as a result of the poor immune function that develops when HIV diagnosis and treatment have been delayed. Therefore, all exposed children require monitoring and prophylaxis for possible HIV infection in addition to routine under 5 care.

Exposed infants must be followed routinely to diagnose (or exclude) HIV infection early, and to provide appropriate prevention, care, and treatment services.

Healthy, exposed children should be monitored according to the under 5 follow-up schedule. Always make sure that a follow-up appointment is given and emphasize the importance of each follow-up visit. See Annex 4 for a detailed follow-up schedule for exposed infants.

Box 3. Minimum follow-up schedule for healthy, exposed infants

Minimum follow-up schedule for healthy, exposed infants	
Immediately postpartum 7-14 days 6 weeks 10 weeks 14 weeks	6 months 9 months 12 months 15 months 18 months
Always make sure that a follow-up appointment is given	

3.2 Routine Comprehensive Care for the HIV-Exposed Child

Routine comprehensive care of exposed infants consists of ten key elements that should be addressed at each child welfare visit. A family based approach is recommended, especially since the health of the infant is correlated with the health of the mother. Encourage involvement of the father. Annex 4 details actions to be taken and counselling for each visit.

Box 4. Ten key elements of an exposed infant visit

Ten KEY ELEMENTS of an Exposed Infant Visit

1) **Document PMTCT regimen received**
2) **Test for HIV or give results, when indicated**
3) **Assess growth and development**
4) **Give immunizations**
5) **Provide prophylaxis (CTX, NVP, IPT)**
6) **Treat infections early**
7) **Ask about household TB contacts**
8) **Counsel on infant feeding and nutrition**
9) **Ensure family is receiving HIV care, FP, social support**
10) **Maintain suspicion for HIV infection**

A. DOCUMENTATION OF PMTCT REGIMEN RECEIVED

Identify PMTCT regimens received by both mother and infant and document them on the child welfare card. This information assists in assessing the risk of infant HIV infection and determines the appropriate ART regimen if the child is determined to be HIV-infected.

B. EARLY INFANT DIAGNOSIS

Provide HIV testing at 6 weeks or as early as possible thereafter. At follow-up visits, ensure that the caregiver has received the child's results and that they are documented on the child health card. Immediately refer all positive infants for ART initiation. For infants who have tested negative, **repeat testing 6 weeks after breastfeeding cessation** or with any signs and symptoms of HIV infection (see testing algorithm in Annex 3).

Box 5. Steps to successful Early Infant Diagnosis and treatment

Steps to Successful Early Infant Diagnosis and Treatment

1) **Record contact info of mother (cell phone or address)**
2) **Reinforce the importance of returning for test results**
3) **Encourage woman to bring partner to discuss test results**
4) **Reinforce that most tests will be negative but for the small number who are positive, initiation of ART should be done urgently to prevent unnecessary morbidity and mortality**
5) **Ensure that counselling/support are available to the family**

C. GROWTH AND DEVELOPMENTAL ASSESSMENT

Check and document weight on the growth curve at each visit to allow for assessment of adequate growth. Mid-upper arm circumference (MUAC) and height should be measured when there is concern for growth failure (Chapter 6). A basic developmental assessment should be done using the chart in Annex 5. Any concern for growth or developmental failure should prompt repeat HIV testing, TB screening, and nutritional intervention.

D. IMMUNIZATIONS

Give immunisations according to the recommended schedule to all HIV exposed and infected infants. However, if a child who has confirmed HIV infection never got BCG initially, the BCG should be withheld. Vitamin A and albendazole should also be given at appropriate intervals.

E. PROPHYLAXIS

Provide nevirapine, cotrimoxazole, and isoniazid prophylaxis when indicated. Nevirapine (NVP) should be given to all exposed infants for at least six weeks after birth to prevent post-partum and breastfeeding HIV transmission. Cotrimoxazole (CTX) should be given to all exposed infants starting from six weeks of age to prevent PCP and other potentially fatal infections. Infants exposed to household TB contacts should receive isoniazid (INH) for six months. Details on prophylaxis for HIV-exposed infants can be found in Chapter 3.3 below and dosing and dispensing information is located in Annexes 6 and 7.

F. EARLY TREATMENT OF INFECTIONS

Actively look for and treat infections early according to IMCI guidelines. Refer for higher levels of care if necessary. Remind caregivers to always seek prompt treatment if the child falls ill at home. Delay in treatment can lead to severe morbidity and mortality.

G. TB CONTACTS

Ask if the child has any household TB contacts. Inquire if the caregiver who has brought the child has any TB symptoms. If there are household contacts or a caregiver with symptoms, the child and caregiver should be evaluated for active TB. Children who do not have active TB should be offered INH prophylaxis for six months. Refer to Chapter 7 and Annex 24 for screening tools and algorithms.

H. INFANT FEEDING AND NUTRITION COUNSELLING

Exclusive breastfeeding for six months with the introduction of complementary foods thereafter should be emphasized (Chapter 6). These recommendations minimize the risk of mother to child transmission, prevent malnutrition, and promote optimal growth and development. Personal, food, and water hygiene to prevent common infections should be reviewed. At 12 months, if a nutritionally adequate and safe diet is available, HIV-negative children should be retested with a rapid test to determine if cessation of breastfeeding is advisable (Annex 21). HIV-negative children can stop breastfeeding gradually over one month. HIV-positive children should breastfeed for as long as possible. In circumstances

where a child is being replacement fed, refer to recommendations in Chapter 6 and the Swaziland *Infant and Young Child Feeding Guidelines*.

I. MATERNAL AND FAMILY HEALTH AND WELLBEING

Assess health and psychosocial wellbeing of family members and/or caregivers. The health of exposed infants is directly tied to the health of their caregivers. The child's mother should be referred for CD4, initiation of ART if eligible, and family planning at each visit. All caregivers should be asked about TB symptoms. Offer HTC for any family members who have not tested. Provide psychosocial support to the family.

J. VIGILANCE FOR HIV INFECTION AND RETESTING

Maintain a high level of suspicion for HIV infection. Healthcare providers should watch for growth failure (falling off the growth curve), poor development (delay or loss of developmental milestones – Annex 5), and clinical signs or symptoms suggestive of HIV infection (Annex 1). **If HIV is suspected, the child should be retested**, staged (clinical and immunologic), and presumptively enrolled in HIV care and treatment.

3.3 Prophylaxis for the HIV-Exposed Child

A. NVP PROPHYLAXIS FOR PMTCT

Swaziland has adopted Option A of the 2010 WHO PMTCT guidelines. As part of this strategy, all HIV exposed infants should be offered NVP prophylaxis for at least six weeks postpartum. The duration of the NVP prophylaxis will then depend on whether the mother is on ART or received AZT prophylaxis during pregnancy, and whether the infant is breastfeeding or not. If the mother is eligible for ART, but has not yet initiated therapy, she should be referred for initiation as soon as possible. Infants eligible for NVP prophylaxis who have not been receiving it should be initiated or re-initiated. Criteria for initiation and duration of extended NVP prophylaxis are described in Table 5 below.

At each visit, mothers should be counselled on the reason for NVP prophylaxis, reminded about the importance of adherence, and instructed on correct dosing. See Annexes 6 and 7 for detailed dosing and dispensing information. Further, if the mother was initiated on ART since the previous visit, or the infant stopped breastfeeding, a plan for discontinuation of NVP and/or retesting of the infant should be made.

Table 5. Criteria and special considerations for infant extended NVP prophylaxis

Infant NVP prophylaxis based on maternal PMTCT regimen	
Maternal PMTCT	**Infant NVP prophylaxis**
On ART	NVP until 6 weeks of age
Received AZT prophylaxis or nothing	Breastfeeding**:** NVP until 1 week after breastfeeding stops Non-breastfeeding**:** NVP until 6 weeks of age
Special Considerations for Infant NVP prophylaxis	
Situation	**Recommendation**
Mother initiates ART during breastfeeding	Infant continues on NVP prophylaxis for at least 6 weeks after the mother initiates ART, or until 1 week after breastfeeding cessation, whichever comes first.
Child defaulted NVP prophylaxis	Counsel on importance of ongoing prophylaxis and restart NVP
Child was never initiated on NVP, is breastfeeding, and mother is not on ART	Review results of any previous HIV test for the infant: • Positive → refer for ART care; do not initiate NVP • Negative → initiate NVP unless child is sickly • Never tested → test for HIV per algorithm and initiate NVP unless child is sickly If child sickly, test or retest for HIV per algorithm and withhold NVP until HIV status is confirmed.

Potential NVP Prophylaxis Toxicities

NVP prophylaxis has very little potential to cause side effects. However parents should be counselled that if the infant develops a severe rash (that includes sores in the mouth and red eyes), they should bring the child to the nearest health facility for evaluation. Toxicities to NVP prophylaxis are very rare and include severe rash and jaundice. However, infants are more likely to develop these symptoms for reasons other than NVP. Consequently, infants who develop a severe rash or jaundice should be referred to a physician for further evaluation and decision about whether or not to continue the NVP.

Confirming Infant HIV Status

NVP prophylaxis reduces the risk of postpartum HIV transmission by over 60%. However, some children can still become infected. At any time, if a child has signs or symptoms of possible HIV infection, retest the child. Further, when the child is no longer breastfeeding, an HIV test should be conducted to determine the child's definitive status. See the Early Infant Diagnosis (EID) Testing Algorithms (Annex 3) for details.

B. COTRIMOXAZOLE PROPHYLAXIS

Cotrimoxazole (CTX) should be given to all exposed infants from 6 weeks of age until HIV infection has been definitively ruled out (Chapter 2) AND the child is no longer breastfeeding. It is a broad-spectrum, inexpensive, and life-saving antibiotic in the HIV context. The effectiveness of CTX prophylaxis has been demonstrated to prevent the incidence and severity of Pneumocystis jiroveci pneumonia (PCP), the leading cause of death in infants with HIV infection. The incidence of PCP peaks in the first 6 months of life and accounts for 50-60% of AIDS diagnoses in infants. CTX also significantly reduces morbidity and mortality from other pathogens among infants and children living with or exposed to HIV.

Give CTX from 6 weeks of age until HIV infection has been definitively ruled out AND the child is no longer breastfeeding.

CTX is generally well tolerated by infants. However parents should be counselled that if the child develops a severe rash (that includes sores in the mouth and red eyes), they should bring the child to the nearest health facility for evaluation. In the rare circumstance that a child has a history of a severe (Grade IV) adverse reaction to CTX or other sulfa-containing drugs, or known severe kidney disease (creatinine > 3 times normal) and/or hepatic disease (LFTs > 5 normal), CTX should be avoided. Dapsone at a dose of 2 mg/kg once daily can be given as an alternative in these circumstances. See Annex 8 for CTX prophylaxis information, including dosing, in exposed infants and children.

C. INH PROPHYLAXIS FOR CHILDREN WITH KNOWN TB CONTACTS

HIV exposed infants who live with someone (especially an adult) with active TB are at risk for TB infection. They should be investigated for TB and if TB is excluded, should receive isoniazid (INH) prophylactic therapy (IPT) for six months at a dose of 10mg/kg. Pyridoxine (1-2mg/kg) should be given to prevent side effects of the INH. See Chapter 7 and Annex 24 for more details about IPT and dosing. Children receiving IPT should be monitored closely for the development of active TB.

Infants with household TB contacts should be given IPT for 6 months after active TB infection has been excluded.

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Chapter 4 Care and Treatment of the HIV-Infected Child, Including ART

Every HIV-infected child has the right to comprehensive therapy, including antiretroviral therapy (ART) when appropriate. In the era of ART, HIV must be treated as a chronic condition. Physical, psychological, and emotional wellbeing should be evaluated on a routine basis. Further, it is crucial that care and treatment are conducted in the context of the family unit.

This chapter provides information for clinicians on:

- Assessment of an HIV-infected child
- ART initiation in infants and children
- Preparation of patient and treatment supporter for lifelong therapy
- ART regimens to use in infants and children
- Monitoring children on ART
- Detecting and managing adverse effects of ART
- Detecting and managing treatment failure

10.1 Assessment of an HIV-Infected Child

Upon diagnosis, children need thorough medical and psychosocial evaluations. This will ensure initial stabilization and proper initiation of ART. Thereafter, routine assessment will assist in:

- Evaluating response to therapy
- Diagnosis of any new conditions
- Monitoring for short- and long-term side effects of treatment
- Assessing changes in the family unit that might affect the child's care
- Ensuring that the child's understanding of his/her condition evolves as the child matures

A summary of key assessment components can be found in Table 6.

Table 6. Assessment of HIV-Infected Infants and Children

Assessment Component	Key questions and evaluations
Medical History	At initial visit: • Birth history, including maternal and infant PMTCT • Past medical history, including TB history • Any previous ART regimens and adherence history At initial and each subsequent visit: • Presenting complaint, if any • Review of symptoms • Growth and developmental history (Annex 5) • Nutritional history (Chapter 6) • Family/household history • Allergies • Medications and traditional remedies
TB Screening (Chapter 7)	• TB contacts? • Cough for >2 weeks? • Fevers for >2 weeks? • Night sweats > 2 weeks? • Noticeable weight loss > 4 weeks?
Psychosocial Assessment (Chapter 9)	• Identify caregivers for child • Disclosure to child and family members • Child and caregiver fears/concerns • Child's understanding of HIV • Child's education and socialization • Adherence to therapy
Complete Physical Examination	• Weight and height plotted on growth curves • Head circumference (children < 2y) – may be indicative of cognitive or developmental delay • Head-to-toe examination of all systems, looking for signs of HIV disease and opportunistic infections
Laboratory Testing (Chapter 4.5A)	• CD4 • Liver function tests and full blood count • Viral load if available (or DNA PCR for those <18m, if viral load not available) • Pregnancy test for adolescent girls
Staging	• Clinical – Annex 9 • Immunologic – Chapter 4.4C

4.2 Prophylaxis for HIV-Infected Children

A. COTRIMOXAZOLE

Cotrimoxazole (CTX) is an inexpensive and life-saving antibiotic in the HIV context. It is a broad-spectrum antibiotic with activity against a wide range of pathogens including *Pneumocystis jiroveci* pneumonia (PCP), Pneumococcus, non-typhoid *Salmonella*, *Isospora*, *Cryptosporidia*, *Nocardia*, *Plasmodium falciparum*, and *Toxoplasma gondii*. The effectiveness of CTX prophylaxis has been demonstrated to prevent the incidence and severity of PCP and reduce morbidity and mortality among children living with HIV.

All children living with HIV should receive CTX prophylaxis for life.

All children with HIV should receive CTX prophylaxis for life. CTX should not be started, or should be discontinued, if the child has:

- A severe (Grade IV) adverse reaction to CTX (Annex 8) or other sulfa-containing medications.
- Severe kidney disease (creatinine > 3x normal) and/or liver disease (LFTs > 5x normal).

In these circumstances, dapsone (2mg/kg once daily) should be used as an alternative.

If a child is overburdened by a large number of tablets, discontinuation of CTX may be considered if:

- the child is over five years, AND
- there is evidence of immune recovery (CD4 > 350 for at least 6 months), AND
- there is NO history of PCP or toxoplasmosis.

B. ISONIAZID PREVENTIVE THERAPY

Isoniazid (INH) preventive therapy (IPT) is recommended for all HIV-infected children in Swaziland. Active TB disease must be ruled out prior to IPT. A screening algorithm to identify patients that qualify for IPT is provided in Annex 24. A more detailed discussion of IPT can be found in Chapter 7.

4.3 Care and Monitoring for the Child Not Yet ART-Eligible

HIV-infected children should be evaluated every 3-6 months for ART eligibility. Children under 5 and children close to immunologic threshold for initiation (Chapter 4.4C) should be monitored every 3 months. Evaluation includes:

- Interim medical history (any new conditions that would change the clinical stage)
- Nutritional assessment (growth failure – wasting or stunting – is often the first sign of active HIV infection)
- TB screening
- Psychosocial evaluation (as children mature, disclosure issues need to be addressed. Family situations and support for the child also often change)
- CD4

4.4 When to Initiate ART

The goal of ART is to restore immunologic function and quality of life, and to increase life expectancy by decreasing morbidity and mortality due to HIV infection. Decisions on when to start ART are based on **age, clinical, immunologic, and social criteria.**

A. INFANTS AND CHILDREN UNDER 2 YEARS

Early Antiretroviral Therapy (EAT):
All infants and children less than 24 months with confirmed HIV infection should be started on antiretroviral therapy, irrespective of clinical or immunologic stage (Table 7). By two years of age, over half of HIV-infected children will die in the absence of treatment. Clinical research shows that early initiation of ART decreases HIV-related infant mortality by 75%[16]. The new recommendation to initiate all children 12-24 months is based on observational studies in developing countries[17].

All HIV infected children less than 24 months should be initiated on ART.

Presumptive Diagnosis:

A presumptive diagnosis of HIV can be made in children less than 18 months using WHO clinical criteria alone (Chapter 2). Children with a presumptive diagnosis should be initiated on ART without waiting for virologic confirmation of infection, because of the associated high mortality in untreated cases. However, HIV infection should be confirmed as early as possible using DNA PCR. ART should be closely monitored and should only be stopped when the child is no longer exposed to HIV (i.e., through breastfeeding from an HIV-infected mother), and when HIV infection can be confidently ruled out.

B. CLINICAL STAGING

HIV-infected children should be clinically staged at every visit. This helps to:

- Monitor the clinical progression of disease
- Inform decision-making on commencement of ART
- Monitor clinical improvement on ART
- Assist in providing a prognosis for the child

Annexes 9 and 10 provide the HIV-related conditions for clinical staging and diagnostic criteria and management of these conditions in infants and children.

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[16] Newell et al, 2004, Spira et al, 1999, Violari et al, 2008.

[17] While clinicians are encouraged to initiate all children under 24 months, it may be reasonable to delay treatment in a child 12-24 months old if the child is not clinically or immunologically compromised, and if close clinical follow-up and consistent laboratory monitoring is available.

All children with WHO clinical stage 3 or 4 should be initiated on ART regardless of CD4/CD4%. For children with WHO clinical stage 1 or 2, initiation of ART is guided by CD4/CD4% (Chapter 4.4C). All infants and children under two years should be initiated on ART regardless of clinical stage. Table 7 provides a summary of when to initiate ART based on clinical criteria.

Table 7. Clinical Criteria for Initiating ART in Infants and Children

Clinical Criteria for Initiating ART in Infants and Children		
	WHO Clinical Stage 1-2	**WHO Clinical Stage 3-4**
Infants and children under 24 months	Treat all	
Children 2-14 years	CD4 guided	Treat all

C. IMMUNOLOGIC STAGING

Children with severe immunosuppression based on CD4 level should be initiated on ART regardless of clinical stage (Table 8). The CD4 criteria for severe immunosuppression in infants and children changes with age. Children under 24 months have a high mortality risk regardless of CD4%, so a CD4 threshold cannot be set. For children 2 years and older, criteria for severe immunosuppresion correspond to a 12-month mortality risk of up to 5%[18]. A CD4 threshold of ≤25% (or ≤750, if % not available) should be used to initiate children ages 2-4.9 years, while a CD4 count of ≤350 should be used to initiate children 5 years and over.

Table 8. Immunologic Criteria for Initiating ART in Infants and Children

Immunologic Criteria for Initiating ART in Infants and Children			
Age	**Infants and children under 24 months**	**2 to 4.9 years (24 – 59 mos)**	**5 years and over**
% CD4	Initiate All	≤25%	≤350 (as in adults)
Absolute CD4		≤750	

[18] Dunn, D. (2003). "Short-term risk of disease progression in HIV-1-infected children receiving no antiretroviral therapy or zidovudine monotherapy: a meta-analysis." Lancet 362(9396): 1605-11.

D. SOCIAL CRITERIA

A primary caregiver, as well as a secondary caregiver whenever possible, must be identified for children initiating ART in order to ensure good adherence and treatment success.

Primary caregivers must assume responsibility for:

- Giving medications regularly
- Bringing the child for follow-up visits
- Providing ongoing general care of the child (nutrition, immunizations, etc.)

Secondary caregivers must be identified to ensure good continued support for the child if the primary caregiver is not available.

Caregiver(s) should be properly counselled and adequately prepared for ART. The primary caregiver should be strongly encouraged to bring the secondary caregiver to the ART initiation visit; however, the unavailability of a secondary caregiver should not delay ART initiation if the HCW feels that a strong support system is in place (Chapter 4.5B). If the child fails ART, re-involving the secondary caregiver in preparations for the next regimen is crucial for success.

E. SUMMARY OF WHEN TO START ART IN INFANTS AND CHILDREN

Box 6. Summary of paediatric ART initiation eligibility criteria

Initiate ART for HIV infected children:

- **Under 2 years, regardless of clinical or immunological stage.**
- **With clinical stage 3 or 4 disease, irrespective of CD4.**
- **With severe immunosuppression, irrespective of clinical stage.**
- **Less than 18 months with a presumptive diagnosis of HIV.**

ART should ideally be initiated within two weeks of qualifying for therapy. This timeframe allows both the family and health care providers time to address disclosure, provide adherence counselling, complete TB screening, and prepare for uninterrupted treatment. Delaying ART in children who meet the criteria, especially in infants and young children, may lead to preventable morbidity and mortality.

Once children meet eligibility criteria, they should be initiated on ART as soon as possible, preferably within two weeks.

4.5 Preparation for ART

When criteria for ART are met, clinical assessment, baseline laboratory tests, and counselling should be expedited to facilitate ART initiation as soon as possible. Clinically, it is also essential to identify, treat and stabilise any opportunistic infections (OIs) before initiating ART (Chapter 5 and Annex 10).

Identify and treat opportunistic infections BEFORE initiating ART.

A. BASELINE LABORATORY TESTS

The following laboratory investigations should be done prior to initiating ART:

Table 9. Baseline Laboratory Investigations

Recommended Baseline Laboratory Tests	
CD4	
FBC	Hb at minimum
AST/ALT	If no signs of liver disease, not required for initiation
Serum Creatinine	If considering use of TDF
Pregnancy test	For adolescent females who have begun menses
Viral Load	For children under 18 months. If viral load not available, a repeat DNA PCR should be done to document two positive virologic tests. The repeat DNA PCR should not delay initiation of ART.

B. PRE-ART ADHERENCE COUNSELLING

Adherence is a process where a patient, in partnership with the medical team, takes their medication as instructed by the health care provider. It involves patients' active participation in their own treatment plans, and the involvement of family members and of community-based support structures where possible.

In the case of children, pre-ART preparation necessitates identifying primary and secondary caregivers before ART is initiated. These caregivers must be willing to supervise the child with his/her treatment, display commitment to his/her care, and understand the importance of consistent follow-up. When the primary treatment supporter is unable to assist the child, the responsibility falls on the secondary treatment supporter to do so. If a second treatment supporter is not available, the risks and benefits of initiating therapy will need to be weighed to determine whether or not to rely upon a single caregiver.

Primary and secondary caregivers should be identified and counselled for all children initiating ART.

Children and their treatment supporters should be counselled on ART adherence prior to initiation. The first pre-ART counselling session should be provided at diagnosis. One to two additional counselling sessions should be conducted in preparation for ART. In general, one to two group sessions followed by an individual session will provide ample time for the provision of information and assessment of readiness for initiation and lifelong treatment. Comprehensive pre-ART counselling should include information on HIV, ARVs, adherence, and positive living. In addition, caregivers and treatment supporters should have a long-term plan to ensure adherence to ART before treatment is initiated. Detailed information on topics to cover can be found in the Comprehensive Package of Care for Adults and Adolescents, and in Annex 11. Once the caregivers have completed adherence counselling successfully, ART should be initiated as soon as possible.

Patients and caregivers must be well-prepared for ART to avoid treatment failure.

Support of the patient and regular monitoring of adherence is essential. Patients must take 100% of their pills to minimize the emergence of drug resistance. Adherence often wanes the longer a patient has been on treatment and most occurrences of treatment failure are due to poor adherence. Consequently, counselling of patients on treatment should be ongoing. See Chapter 9 for more information about adherence counselling.

Adherence counselling and support should be provided on an ongoing basis and key messages repeated regularly.

4.6 Antiretroviral Therapy (ART) for Children

A. BACKGROUND: ARVS AND HOW THEY WORK

Antiretroviral drugs (ARVs) inhibit the process of viral replication. Three main classes of ARVs are used, each of which has a different action.

Table 10. ARV Medication Classes and Mechanisms of Action

ARV Medication Classes and Mechanisms of Action		
ARV Class	**Mechanism of Action**	**Examples**
Nucleoside reverse transcriptase inhibitors (NRTIs)	Attach to the RNA strand and shorten the transcription of DNA from RNA by the reverse transcriptase enzyme.	Zidovudine (AZT) Stavudine (d4T) Lamivudine (3TC) Abacavir (ABC) Didanosine (ddI)
Nucleotide reverse transcriptase inhibitors (NtRTIs)		Tenofovir (TDF)
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Directly inhibit the reverse transcriptase enzyme	Nevirapine (NVP) Efavirenz (EFV)
Protease inhibitors (PIs)	Prevent formation of new viral particles by inhibiting the protease enzyme	Lopinovir/ritonavir (LPV/r)

Antiretroviral therapy (ART), a combination of three ARVs, usually from two different classes, can reduce the viral load to undetectable levels by inhibiting viral replication. Absolute eradication of the virus is not achievable because ARVs are unable to reach the lymphoid tissue or central nervous system that serve as sanctuary sites for HIV. If treatment is stopped, or adherence to medication is poor, the virus will replicate to high levels again. During replication, the virus can readily mutate. Poor adherence leads to low drug levels, consequently increasing the chance that the virus will develop resistance mutations to those ARVs. Therefore, patients should adhere to and continue treatment for life.

B. RECOMMENDED FIRST-LINE REGIMEN

Since publication of the 2006 Swaziland Paediatric Guidelines, much research has been conducted on the effect of PMTCT and the efficacy of different ART treatment regimens in children. Mounting evidence suggests significant resistance to NVP in children who have received prolonged exposure to NVP[19]. As the majority of HIV-exposed infants in Swaziland will be receiving at least six weeks of NVP post-partum to prevent mother to child transmission, those infants who are infected will have a high likelihood of carrying a NVP-resistant strain of the virus. Further, with the new infant feeding and PMTCT guideline recommendation to breastfeed for at least 12 months, many children may be NVP-exposed for longer. Consequently, the recommended first-line ARV regimen for NVP-exposed children

[19] Eshleman SH et al, 2005; Matinson NA et al, 2007; Church JD, et al 2008; NIH bulletin 2009

under 2 years of age in Swaziland is AZT-3TC-LPV/r. For children who are not NVP-exposed, or who are 2-12 years of age, AZT-3TC-NVP is recommended. Children 12 years and older should be initiated on the recommended adult first-line regimen of TDF-3TC-EFV. Specific dosing information for each regimen can be found in Annex 13.

Table 11. Recommended First-Line ART Regimens and Alternative Regimens for Special Situations

Recommended First-Line ART Regimens				
Under 2 years		**2 - 11.9 years**	**12 years and older**	
NVP-exposed	*NOT* NVP-exposed	(Regardless of NVP exposure)	<40kg	≥40kg
AZT – 3TC – LPV/r	AZT – 3TC – NVP	AZT – 3TC – NVP	AZT – 3TC – NVP	TDF – 3TC – EFV
Once initiated, children should continue on their initial regimen for life unless a switch is indicated (e.g., toxicity, development of TB, simplification of regimen, or treatment failure)				

Alternative First-Line ART Regimen Options for Special Situations		
Special Situation	**Alternative Regimen**	**Comments**
Severe anaemia (Hb < 8 g/dl)	Use d4T instead of AZT	Children with non-AZT-induced anaemia should be switched from d4T to AZT once Hb > 10.
TB co-infection	Under 3y or 10kg: AZT – 3TC – NVP	• If child was on ART prior to initiating TB treatment, switch back to original ART regimen after completion of TB treatment (Chapter 7, Table 20) • If child initiated TB treatment before ART, continue regimen initiated during TB treatment. If on EFV, consider switching to NVP after completion of TB treatment to simplify regimen (Chapter 7.5).
	At least 3y and 10kg: AZT – 3TC – EFV	
Children 2-3 years old who received NVP within the last year	AZT – 3TC – LPV/r	If child received extended NVP prophylaxis within the last year, consider LPV/r as the chance of NVP resistance is high.
Failure to demonstrate ability to correctly dose LPV/r syrup	AZT – 3TC – NVP	Close monitoring for clinical, immunologic, and viral failure is imperative.
Children 12 years and older weighing 35-39.9kg	TDF – 3TC – EFV	May use this regimen with the following dosing: TDF/3TC FDC + EFV 400mg

C. SPECIAL CONSIDERATIONS FOR PAEDIATRIC DOSING

Fixed Dose Combination (FDC) Tablets:

Fixed dose combination (FDC) tablets should be used whenever possible as they simplify treatment and improve adherence. Paediatric formulations are crushable and/or dispersible in water, so they can be used at the lowest weight bands. See Annex 12 for available FDC formulations.

Use FDCs whenever possible.

Phasing-Out of d4T:
Swaziland is attempting to phase out the use of d4T due to its many long-term side effects. Any child on d4T who does not have known toxicity to AZT should be switched to AZT as long as the Hb > 10. Only those children who are severely anaemic or who have known toxicity to AZT should remain on d4T. If these children develop d4T side effects, ABC can be used as an alternative.

Substitute d4T with AZT for any child who does not have known toxicity to AZT.

Use of LPV/r: Despite the treatment benefits of an LPV/r-based regimen, the use of LPV/r poses challenges.

- Formulation and dosing: Only syrup formulations are available for infants and children less than 10kg. User-friendly syringes and detailed instruction on dosing should be provided to caregivers. An alternative regimen should be considered for children whose caregivers cannot demonstrate proper use of the syringe, or who routinely spit out the mediation due to poor palatability. More patient- and caregiver-friendly formulations are in development, and should be procured as they become available.
- Storage: In order to maintain potency, facilities must keep LPV/r syrup in medication storage refrigerators at 4^{o}C prior to dispensing. Once dispensed, LPV/r syrup only remains potent for 8 weeks stored at room temperature (25^{o}C). Patients should therefore be given only a two month supply.
- TB co-infection: LPV/r is not recommended in children concurrently being treated for TB. Table 11 above and Chapter 7 list alternative regimens.
- Potential switching option: Switching to an NNRTI-based regimen after a programmed period of LPV/r therapy may be a safe and cost-effective approach that also delays some of the potential long-term metabolic side effects of LPV/r and preserves LPV/r for future use as a second-line drug. Routine virologic monitoring is an essential component of the switch strategy[20]. Taking into consideration the benefits, challenges, and cost of LPV/r-based therapy, Swaziland may consider recommending a switch from LPV/r to an NNRTI for children with confirmed viral suppression for at least six months on LPV/r if reliable, routine virologic monitoring becomes available.

[20] Coovadua A et al. Reuse of Nevirapine in Exposed HIV –Infected Children After Protease Inhibitor-Based Viral Suppression: A Randomized Controlled Trial. *JAMA* 304 (10). 8 Sept 2010. 1082-1089.

Dosing for NVP Initiation:

- Lead-in dosing for routine initiation: Initiation of a NVP-based ART regimen requires a lead-in period of 2 weeks (Table 12) for enzyme induction. During this time, the NVP is dosed once daily to minimize the risk of NVP-related adverse events (severe rash/hepatitis). Initiation packs should be provided to facilitate proper dosing and minimize confusion. After 2 weeks, the dose should be increased to the normal twice daily dosing provided there are no adverse reactions.

Table 12. Example of Lead-in Dosing for routine NVP initiation using AZT-based FDCs

Example of Lead-in Dosing for routine NVP initiation using AZT-based FDCs		
	AM	**PM**
First 2 Weeks	Dual FDC (AZT-3TC)	Triple FDC (AZT-3TC-NVP)
After 2 Weeks (if no adverse reactions)	Triple FDC (AZT-3TC-NVP)	Triple FDC (AZT-3TC-NVP)

- No lead-in dosing: In circumstances where the hepatic enzymes have already been induced, children should initiate NVP at twice daily dosing. Initiating these children at once-daily dosing increases the risk of developing resistance to NVP. Common situations requiring no lead-in dosing include TB/HIV co-infected children taking rifampicin and children switching from EFV or LPV/r to NVP-containing regimens.

Do NOT use lead-in dosing for NVP initiation in patients on TB treatment, or switching to NVP from EFV or LPV/r

- Monitoring for adverse reactions: Whether or not lead-in dosing is used, caregivers should be counselled to return to the facility promptly if the child develops a rash or becomes unwell during the initiation period. Caregivers should be instructed not to stop therapy without authorization from clinic staff. Time to onset of rash is key, with the greatest risk in the first 6 weeks after initiation of NVP. Typically the rash is maculopapular of variable severity and should be graded (Annexs 14 - 16). Although evidence is conflicting, female sex, CD4 count over 250, and viral hepatitis co-infection are considered risk factors in adults for NVP reactions and should be monitored more closely.

D. MONITORING PATIENTS ON ART

Patients on ART need to be monitored with regular clinical and laboratory evaluations to assess response to therapy and possible adverse effects.

Clinical Monitoring

Once an infant or child is on ART, the frequency of clinical monitoring will depend on their response to ART. Standard monitoring should follow the schedule listed in Table 13. Frequent visits during the first three months after initiation are crucial to monitor for the immune reconstitution inflammatory syndrome (IRIS) and acute ART toxicities.

Table 13. Clinical monitoring for patients on ART

Clinical monitoring post-ART initiation	
Visit frequency	**Assess for**
Week 2	• Side effects or toxicity related to ART (Chapter 4.4E) • Improvement in growth and development • Opportunistic infections and/or IRIS (Chapter 5, Annex 10) • Correct dosing of ART (Annex 13) and TB treatment (Annex 25), if receiving both • Adherence • Treatment failure (Chapter 4.4F)
Week 4	
Week 8	
Week 12	
Every 4 weeks for infants less than 12m OR Every 2-3 months for children over 12m, if stable on therapy and adherence is good	

Laboratory Monitoring

Regular laboratory assessment should be focused on monitoring for treatment response and medication toxicity. Labs should be drawn 4 weeks after ARV initiation to evaluate for side effects such as anaemia, liver damage, or renal toxicity. Thereafter, lab monitoring is only required every 6 months or as symptoms or co-morbidities dictate. Based on data in adults on ART, routine monitoring of LFTs in asymptomatic patients is unlikely to be cost-effective[21] and therefore not recommended. The table below summarises the routine follow up visit schedule and laboratory monitoring for paediatric patients on ART.

[21] DART 2010

Table 14. Laboratory monitoring for patients on ART

Laboratory Monitoring for patients on ART				
Laboratory test	**Baseline**	**4 weeks after ART initiation**	**Every 6m**	**As required or symptom-directed**
Haemoglobin	✓	✓[5]	✓[5]	Pallor, fatigue, tachycardia
WBC and differential				Recurrent infections, concern for haematologic malignancy
CD4/CD4%	✓		✓	More frequent if concern for treatment failure
ALT/AST	✓[1]	✓[1]		Jaundice, abdominal pain
Glucose, lipids			✓[6]	Polyuria, polydypsia
Creatinine	✓[2]		✓[2]	Concern for renal failure
HIV viral load	✓[3]			Concern for treatment failure
Pregnancy testing	✓[4]			Concern for pregnancy
Lactate, full chemistry				Concern for lactic acidosis
Lipase				Concern for pancreatitis

[1] If symptomatic (large liver, jaundice, etc), using hepatotoxic drugs (INH, anti-epileptics, etc) or comorbidities (hepatitis B or C, cirrhosis, etc)

[2] If using TDF and have underlying renal disease, hypertension, diabetes, weight <50kg, or are also on a PI. Calculate creatinine clearance = (140-age) x (wt in kg) x (1.23 for men or 1.04 for women) / (72 x Cr in μmol/L). Adjust TDF dose: CrCl≥50 → 300mg OD; CrCl 30-49 → 300mg q48h; CrCl 10-29 → 300mg q72-96h

[3] Use for confirmation of diagnosis in children < 18 months, if available. Otherwise use repeat DNA PCR.

[4] In adolescent girls

[5] If using AZT

[6] If using LPV/r

E. ADVERSE EFFECTS AND DRUG TOXICITY

While ARV medications are highly beneficial, side effects and toxicities are not uncommon. Although data in children are limited, the full spectrum of ARV toxicities observed in adults has also been reported in children[22]. Compared to adults, some toxicities (e.g., NVP-related symptomatic hepatitis) are less common in children, while others (e.g., EFV-related rash or TDF-related loss of bone density) are more commonly reported. HCWs should educate patients to recognize and report common side effects as well as ask patients about possible adverse reactions at routine follow-up visits.

Minor side effects such as headaches, nausea, abdominal pain, diarrhoea and difficulty in sleeping at night usually resolve within 2-6 weeks. They should be managed symptomatically.

Major side effects can be either *acute* or *long-term.*
Grading*:* Whenever a major side effect is recognized, it must be graded to determine the appropriate intervention. Criteria for grading can be found in Annexes 14 and 15.
Substitution: Severe toxicity may require substitution for the culprit ARV. Substitution is the replacement of one drug that has caused toxicity with another drug that does not have the same adverse effects. This is not the same as changing (or switching) to 2nd line for treatment failure. An example is substituting d4T for AZT if anaemia occurs with AZT. Table 15 summarizes the toxicities of the first-line drugs and suggested substitutions. More detailed information on management of toxicities and substitutions can be found in Annex 16.

[22] McComsey and Leonard 2004

Table 15. Severe ARV toxicities associated with first-line regimens and suggested substitutions

Severe ARV Toxicities in children and suggested first-line substitutions			
Most usual ARV cause	**Short Term Toxicity**	**Long Term Toxicity**	**Suggested first-line ARV drug substitution**
NVP	Acute symptomatic hepatitis		EFV
	Hypersensitivity reaction		• A third NRTI (disadvantage: may be less potent) • PI (disadvantage: premature start of class usually reserved for second-line)
	Severe or life-threatening rash (Stevens-Johnson syndrome)		
d4T	Pancreatitis	Peripheral neuropathy	AZT or ABC*
		Lipoatrophy/ metabolic syndrome	ABC*
		Lactic acidosis	
AZT	Severe anaemia or neutropenia	Severe gastrointestinal intolerance	d4T or ABC*
		Lactic acidosis	ABC*
EFV		Persistent and severe central nervous system toxicity	NVP
		Potential terato-genicity in 1st trimester	
ABC	Hypersensitivity reaction		AZT*
LPV/r		Lipoatrophy/ metabolic syndrome	NNRTI
		Dyslipidemia	
		Severe diarrhoea	
TDF*	Renal tubular dysfunction	Renal insufficiency	AZT
		Decreased bone mineral density	
**TDF can be used if the child is at least 12 years and 35kg*.			

F. TREATMENT FAILURE

ART failure is defined as suboptimal response or a lack of sustained response to therapy using clinical, immunologic, and/or virologic criteria (Table 16). The child should have received the ART regimen for at least 24 weeks and had optimal adherence.

Table 16. Criteria for ART failure in children

<table>
<tr><th colspan="3">Criteria for ART Failure in Children</th></tr>
<tr><th>Clinical</th><th>Immunologic</th><th>Virologic</th></tr>
<tr><td rowspan="4">• Lack or decline of growth in a child showing initial response to treatment despite adequate intake
• Loss of neurodevelop-mental milestones or development of HIV encaephalopathy
• New evidence of stage 3 or 4 disease (exclude IRIS)*
• Recurrence of prior opportunistic infections</td><td>2-5 years</td><td rowspan="4">Persistent viral load above 5000 RNA copies/ml, after at least 24 weeks on ART, in a fully treatment-adherent child</td></tr>
<tr><td>CD4 <200 or <10%</td></tr>
<tr><td>Over 5 years</td></tr>
<tr><td>CD4 <100</td></tr>
<tr><td colspan="3">*Short episodes of lower respiratory tract infections and gastroenteritis should not be regarded as treatment failure. Presentation with TB while on first-line therapy is NOT an indication to switch to second-line therapy even though it can present as progression to Stage 3-4 disease.</td></tr>
</table>

Strategies to prevent resistance to first-line ART regimens optimize the success of long-term treatment; however, many factors can lead to suboptimal therapy and put patients at risk of developing resistance to first-line ART.

- **Poor Adherence:** Adherence is the key to successful therapy. In fact, patients with adherence between 70% and 89% have the highest likelihood of developing resistance. Multiple factors including treatment fatigue, multiple caregivers, and social barriers contribute to suboptimal adherence and ultimately to treatment failure.
- **Medication interactions:** Medication interactions may decrease the potency of ARVs, thereby leading to suboptimal therapy. Specifically, patients who have been treated for TB or seizure disorders while taking ARVs are at high risk for treatment failure due to previous or current drug-drug interactions.
- **Incorrect Dosing:** Children are often under-treated due to providers failing to increase the child's dose as the weight increases, or caregiver misunderstanding of dosing. Under-dosing provides suboptimal therapy and consequently predisposes to the development of resistance.

Suboptimal treatment due to any of the above factors can lead to a patient developing opportunistic infections, showing a poor CD4 response, and/or having a high viral load. It is important, therefore, to investigate for and correct these factors when these signs of failure are recognized. If these factors are not corrected, or continue over an extended period of time, they can lead to true ART failure.

If non-resistance causes of failure (poor adherence, under-dosing, or drug-drug interactions) remain unaddressed, ART resistance will eventually develop.

Management of Treatment Failure

When treatment failure is suspected, it is difficult to determine the optimal time to switch to second-line. As stated above, not all instances of presumed treatment failure require an immediate change in antiretroviral therapy. Correction of non-resistance causes of failure such as poor adherence, under-dosing, and drug-drug interactions often provide improvement. A careful step-by-step assessment, preferably involving a multidisciplinary team (MDT), is required to evaluate the aetiology and determine the appropriate management strategy (Box 7 and Annex 17).

Box 7. Steps for Management of Treatment Failure

Five Steps for Management of Treatment Failure

1) **Identify cause(s) of failure**
   - Poor adherence due to psychosocial issues
   - Suboptimal ART levels from under-dosing or drug interactions
   - ART resistance from previous exposure to NVP, previous poor adherence, or previous drug-drug interactions

2) **Provide appropriate intervention**
   - Intensify adherence interventions (Chapter 9.5)
   - Correct medication doses or minimize drug-drug interactions
   - Treat gastroenteritis and opportunistic infections

3) **Continue or restart CTX, or other indicated prophylaxis**

4) **Confirm suspected failure with viral load, if available**

5) **If, after a careful evaluation, non-resistance causes of failure (poor adherence, drug-drug interactions) are not identified, then assume that resistance has developed and change to second-line regimen.**

G. SECOND-LINE THERAPY

When to Switch to Second-Line

Changing from first- to second-line ART is a decision that is undertaken only after careful consideration. It should not be rushed before considering possible improvements in managing therapy at home. Second-line regimens usually have a greater pill burden, are more expensive, and are more demanding for the child's adherence compared to first-line regimens. Delayed switching to second-line, however, allows for the development of

resistance to multiple NRTIs and has the potential to undermine the potency and durability of second-line options. Therefore, although it is important and desirable to preserve the first-line regimen for as long as possible, switching to a second-line regimen should be done as soon as it is determined that the child is truly failing and a good adherence and support plan can be made with the family and with the child's other care providers. Discussions within the multidisciplinary team (MDT) will facilitate this decision.

Only switch to second-line when issues of disclosure, adherence, and treatment support have been fully addressed.

Recommended Second-Line Regimens

New second-line regimens emphasize use of FDC formulations to facilitate adherence. While 2006 guidelines included ddI in the 2nd line regimen, new recommendations utilize 3TC instead of ddI. Not only is 3TC part of the FDC formulations, it also reduces viral fitness.

Table 17. Recommended Second-Line Regimens

<table>
<tr><th colspan="3">Recommended second-line treatment in cases of treatment failure</th></tr>
<tr><th>1st line regimen</th><th colspan="2">Preferred second-line</th></tr>
<tr><td></td><td>Children under 12 years</td><td>Children 12 years and older</td></tr>
<tr><td>AZT – 3TC – NVP
d4T – 3TC – NVP
AZT – 3TC – EFV
d4T – 3TC – EFV</td><td>ABC – 3TC – LPV/r</td><td>TDF – 3TC – LPV/r
or
ABC – 3TC – LPV/r
(if < 35kg)</td></tr>
<tr><td>AZT – 3TC – LPV/r
d4T – 3TC – LPV/r</td><td colspan="2">ABC – 3TC – NVP*
or
ABC – 3TC – EFV*</td></tr>
<tr><td>TDF – 3TC – NVP
TDF – 3TC – EFV</td><td>N/A</td><td>ABC – 3TC – LPV/r
or ATV/r</td></tr>
<tr><td colspan="3">*If a child on a LPV/r first-line regimen experiences treatment failure, second-line options are limited. An NNRTI will likely need to be used as the second-line regimen of choice. Consultation with an expert should be obtained.</td></tr>
</table>

Children Currently on Second-Line Regimens

Many children are currently on second-line regimens that include ddI. If these children are thriving and have good adherence, they may continue on ddI. If they are doing poorly, have poor adherence, or desire a smaller pill burden, ddI can be substituted for 3TC so that FDC tablets can be used.

Chapter 5 Management of Common Childhood Illnesses and Opportunistic Infections in HIV-Exposed and Infected Children and Adolescents

5.1 Introduction

This section provides an approach to the management of common childhood illnesses and opportunistic infections (OIs) in HIV-exposed and infected children and adolescents, adapted from the *WHO Integrated Management of Childhood Illness (IMCI)* guidelines. There are unique considerations for this group of patients, including differences from adults in mode of acquisition, natural history, diagnosis, and treatment. The guidelines consider OI treatment for both HIV-exposed and infected children. HIV-exposed but uninfected infants may be affected by OIs if they are infected with pathogens from their mothers or family members.

OIs in children often present differently than in adults.

The natural history of OIs among children might differ from that among HIV-infected adults. Often, OIs in adults are due to reactivation of pathogens acquired before HIV infection. However, OIs among HIV-infected children more often reflect primary infection with the pathogen. In addition, because perinatally-acquired HIV infection progresses rapidly in most children, the immune system may already be compromised. These factors contribute, for example, to the fact that young children with TB are more likely than adults to have extra-pulmonary and disseminated infection.

Diagnosis of OIs is difficult in children. Children may be unable to describe the symptoms of disease, diagnosis in infants is complicated by the presence of maternal antibodies, and assays capable of directly detecting pathogens are often costly and time-consuming.

Treatment in children may be complicated and is often based on data related to studies in adults. Issues related to drug pharmacokinetics, formulation, ease of administration, and dosing and toxicity require special considerations for children. Further, some OIs are not curable with current therapy and require ongoing secondary prophylaxis after treatment. Sustained and effective ART, resulting in improved immune status, has been established as the most important factor in controlling OIs among both HIV-infected adults and children. Annex 18 contains paediatric dosing of many commonly available medicines in Swaziland.

ART is the most important factor in controlling OIs.

In this chapter common OIs are described by system: respiratory, gastrointestinal, constitutional (fever), dermatologic, and neurologic. For each OI, the following are reviewed:

- Key points
- History/symptoms
- Physical signs
- Investigations
- Management

5.2 Cough or Difficulty Breathing

All children can have a cough related to upper respiratory infections, bronchitis, and even viral croup. However, HIV-exposed/infected children are at risk of more severe infections and should always be assessed for danger signs according to the IMCI guidelines. Treat or refer for advanced care as needed. Specific OIs that should be considered in all HIV-exposed/infected children presenting with cough or difficulty breathing include:

- Bacterial/viral pneumonia
- Pulmonary Tuberculosis (TB)
- Pneumocystis Pneumonia (PCP)
- Lymphoid Interstitial Pneumonitis (LIP)

A. PNEUMONIA IN HIV-EXPOSED/INFECTED CHILDREN

Key Points

- HIV exposed/infected children are at increased risk of developing pneumonia.
- Rapid response to medications (including CTX) within 3-5 days suggests susceptible bacterial or responsive allergic aetiologies for respiratory problems.
- Delayed responses after 5-7 days would favour TB or PCP though other disorders (e.g., foreign body, complicated bacterial pneumonias, inappropriate antibiotics, resistance organisms, asthma, underlying LIP, bronchiectasis) need to be evaluated.

History/Symptoms

- Acute or subacute onset of fast breathing, cough, and fever (as in HIV-negative children).

Physical Signs

- Tachypnea, dyspnea, retractions, flaring, crackles, rhonchi, dullness to percussion.

Investigations

- Chest x-ray if needed. Children 6 years and over may be able to produce a sputum specimen.

Management

- Provide routine antibiotic treatment such as high-dose amoxicillin (80-100mg/kg/day divided BD or TDS).
- Strongly consider high dose CTX (TMP 5 mg/kg + SMX 25 mg/kg 4 times/day for 21 days) in all HIV-exposed/infected infants under 12 months of age with features of severe pneumonia to cover for PCP (see below).

B. TUBERCULOSIS

Key Points

- Since the reported seroprevalence of HIV in children with TB ranges from 10 to 60%, it is important to consider TB in a child with proven or suspected HIV.
- TB is the most common cause of death in children with HIV. The diagnosis of TB must be considered prior to the initiation of ARVs.
- A diagnosis of any form of TB (pulmonary, lymph node, or extrapulmonary; clinical stage 3 and 4 conditions) indicates ART should be started.
- See Chapter 7 for details on TB/HIV co-management.

TB is a clinical stage III or IV condition requiring ART.

C. PNEUMOCYSTIS JIROVECI PNEUMONIA (PCP)

Key Points

- If untreated, mortality due to PCP can be as high as 100%. Therefore it remains imperative to have a high index of suspicion for PCP and to diagnose and treat as early as possible. Irrespective of additional diagnosis (i.e., bacterial pneumonia, asthma, LIP, Pulmonary TB, etc.) in a child with cough or difficult breathing it is essential to consider co-infection and treat.
- Response usually takes more than 5-7 days of appropriate high-dose cotrimoxazole (CTX) therapy.

PCP is a clinical stage IV condition requiring ART.

History/Symptoms

- Suspect PCP in all HIV-exposed/infected children but especially in:
  - All infants under 12 months.
  - Infants or children irregularly using or not on CTX prophylaxis.
  - Children with CD4/CD4% below severe immunosuppression thresholds.
- Sub-acute or acute onset of non-productive cough and difficulty breathing.
- Fever (usually mild).

Physical Signs

- Respiratory distress (tachypnea, chest indrawing, etc.).
- Hypoxia disproportionate to findings on auscultation (which usually shows normal breaths sounds or bilateral crepitations/rhonchi).

Investigations

- CXR will typically show a bilateral diffuse interstitial reticulogranular ("ground glass") pattern with no hilar lymph nodes or effusions. PCP may also present with pneumothorax. In 10-20% of cases, CXR will be normal.

Management

- High dose CTX, corticosteroids and oxygen therapy should be provided. See Annex 10 for details on treatment.
- Initiate ART.
- Once PCP treatment is complete, CTX prophylaxis should be given for life as per usual prophylaxis dosage guidelines (Chapter 3 and Annex 8).

D. LYMPHOID INTERSTITIAL PNEUMONITIS (LIP)

Key Points

- LIP is a lymphoproliferative, non-infectious pulmonary disorder that is characterized by diffuse infiltration of CD4 lymphocytes, plasma cells, and histiocytes in alveolar septa and along the lymphatics.

- It is most common in children infected with HIV, especially those over 3 years old.

Symptomatic LIP is a clinical stage III condition requiring ART.

History/Symptoms

- Chronic cough unresponsive to treatment.

Physical Signs

- Clubbing, stunted growth, generalized lymphadenopathy, bilateral parotid enlargement, hepatosplenomegaly.
- Features of cor pulmonale (cough/breathlessness, raised JVP, tender hepatomegaly, bilateral pitting pedal oedema, prominent 2nd heart sound on auscultation of pulmonary area).
- Chest auscultation usually normal although often diffuse crepitations and/or rhonchi are heard.

Investigations

- CXR: bilateral reticulonodular interstitial pulmonary infiltrates usually more prominent in lower lobes. See Annex 10 for more details.

Management

- Bronchodilators are useful in mild-moderate symptomatic children, especially those with wheezing.
- Corticosteroids (oral prednisone) – see Annex 10 for dosing.
- ART initiation should be strongly considered for those not yet on treatment.

5.3 Diarrhoea and Other Gastrointestinal Problems

Diarrhoea is one of the most common manifestations of HIV in children, especially in infancy. Prevention of diarrhoea is important and caregivers of HIV-infected children should pay particular attention to personal hygiene (hand-washing), drinking boiled water, and eating only thoroughly-cooked meat and cooked or thoroughly-washed fruits and vegetables. While most children have acute diarrhoea, some will present with persistent (or chronic) diarrhoea.

A. ACUTE DIARRHOEA IN HIV-INFECTED CHILDREN

Key Points

- Acute diarrhoea should be approached as in non-HIV infected children.
- Assessment and correction of dehydration is the most important aspect of care, as dehydration poses the most imminent mortality threat.

History/Symptoms

- Are there danger signs? (IMCI – Ask, Look, Feel)
- Is there Diarrhoea? (Frequency of stools, consistency of stools)
- Is there Persistent Diarrhoea? (Diarrhoea >14 days)

Physical Signs

- Is the child dehydrated? (IMCI – Ask, Look, Feel)
  A child who is not making tears when crying indicates moderate to severe dehydration and requires aggressive management.
- Is there blood in stools? (Diarrhoea containing blood)

Investigations

- If severely dehydrated or malnourished, a chemistry panel may be helpful.

Management

- Classify using IMCI (Ask, Look, Feel) into no, some, or severe dehydration.
- Urgently manage dehydration with oral rehydration solution (ORS) or IV infusion, depending on the dehydration status, per IMCI guidelines.
- Once stable, advise parents to give the child more fluids than usual, to prevent dehydration.
  - Advise to drink more fluids from onset of diarrhoea. Encourage children to drink as much as possible – they may not feel thirsty so keep water by bed and encourage small regular sips.
  - Advise on how to make ORS using clean boiled water.
- Continue to feed the child, to prevent malnutrition.
  - Encourage children to eat! Advise caregivers to give an extra meal per day for two weeks to help with regaining lost weight.

- A diet low in lactose or lactose-free may be indicated until the intestinal mucosa recovers.

- Treat the underlying cause (particularly if there is dysentery (loose stool containing blood) or if the diarrhoea is suggestive of cholera or giardiasis.
- Provide zinc 10mg (if <10kg) or 20mg (if >10kg) once daily for 10 days.

The most important aspect of managing diarrhoea is correcting dehydration with ORS or IV infusion.

B. PERSISTENT DIARRHOEA IN HIV-INFECTED CHILDREN

HIV-infected children, as mentioned, are prone to persistent diarrhoea. Differential diagnosis of persistent diarrhoea in children infected with HIV includes opportunistic infections (viral, bacterial, protozoal/parasitic), secondary conditions (allergies, lactose intolerance), HIV-related medication side effects, and nutritional deficiencies. Proper care of HIV-infected children with persistent diarrhoea is therefore essential.

Key Points

- Persistent or chronic diarrhoea is described as diarrhoea (loose or watery stools, >3 times a day) of >2 weeks duration.
- Persistent diarrhoea is associated with an 11-fold increase of risk of death in HIV-infected infants.

Persistent diarrhoea is a clinical stage III condition requiring ART.

History/Symptoms

- Review questions listed under acute diarrhoea.
- Small quantity mucoid stool with blood, especially with tenesmus, indicates a probable colitis. Typical aetiologies are *Shigella*, ameobiasis, CMV, *Campylobacter jejuni* and *Clostridium difficile*.
- Predominately watery explosive stools, or diarrhoea associated with steatorrhea, flatulence, and fat malabsorption point to a small intestine diarrhoea. Causes included lactose intolerance, *Giardia lamblia*, *Mycobacterium avium* complex (MAC), *Cryptosporidium*, non-typhoid *Salmonella*, *Microsporidia*, *Isospora bella* and *Camplylobacter*, and specific treatments will be used empirically as per a treatment algorithm.

Physical Signs

- Evaluate hydration status: A child who is not making tears when crying indicates moderate to severe dehydration and requires aggressive management. Dehydration in a child with persistent diarrhoea indicates IMCI-classified Severe Persistent Diarrhoea.

- Look for blood in the stool.
- Look for signs of fat-soluble vitamin (A,D,E,K) deficiencies.

Investigations

- Stool studies where possible (ova, parasites, culture).
- Fecal occult blood; stool smears.

Management

Since it is difficult to distinguish the different causative agents of persistent diarrhoea without stool culture, an empiric approach to treatment is recommended in immunocompromised children with persistent diarrhoea.

- Follow steps under acute diarrhoea for management of the acute episode.
- Initiate ART as soon as possible: ART and improvement in the immune status of the child may be the only way to improve persistent diarrhoea.
- Empiric oral antibiotic treatment:
    - For diarrhoea with blood: ciprofloxacin 15 mg/kg BD x 3 days AND metronidazole 5-10 mg/kg TDS x 7 days.
    - For small bowel watery persistent diarrhoeas: CTX (TMP 5 mg/kg + SMX 25 mg/kg) every 6 hours AND metronidazole 10 mg/kg TDS x 10-14 days.
    - If no response to treatment, refer for higher level of care.

DO NOT USE anti-motility agents (e.g., loperamide) in children with infectious diarrhoea

5.4 Fever

Causes of fever in HIV-infected children are often similar to causes of fever in HIV non-infected children. Clinical presentations, however, may be atypical and the course prolonged. The risk of septicaemia is 2.5 times that of HIV-negative children. Just like fever, aetiology can vary widely and a high level of suspicion is critical.

Due to the risk of rapid progression of infectious aetiologies in HIV-infected children, any fever requires prompt diagnosis and interventions. All HIV-infected children should first be assessed for danger signs, as per IMCI.

A. PERSISTENT OR RECURRENT FEVER

Persistent fever is a temperature more than 37.5^{o}C on 2 occasions within 5 days, and is significant. Causes include:

- Occult bacterial infections (sinusitis, otitis media, urinary tract infection, osteomyelitis, abscess, septicaemia [*Salmonella, Streptococcus pneumoniae, Hemophilus influenzae*], endocarditis, liver abscess).
- Mycobacterial – tuberculosis, *M. avium*.

- Fungal – candidiasis.
- Viral – Epstein-Barr Virus (EBV).
- Parasitic – malaria.

Persistent fever of unknown origin is a clinical stage III condition requiring ART.

History/Symptoms

- General danger signs:
    - Is the child able to drink or breastfeed?
    - Does the child vomit everything?
    - Has the child had convulsions?
- If the main symptom is fever (T=37.5^{o}C and above), find a focus. Causes may include otitis media, pneumonia, diarrhoea, malaria, or HIV infection itself.

Physical Signs

- Fully undress the child and examine the whole body for any localizing signs of infection to identify the focus.
- Some causes of persistent fever may have no localizing signs. In those cases, you need to be highly suspicious of septicaemia, *Salmonella* infections, miliary tuberculosis, HIV infection, or urinary tract infection.
- Signs of sepsis include shock (low pulse volume, tachycardia, hypotension, prolonged capillary refill, decreased urine output, altered consciousness) and possibly bleeding (DIC) and skin eruptions.

Investigations

- Consider blood count, smear for malaria, blood culture, CSF analysis, stool microscopy, CXR, and/or urinalysis.

Always maintain a high index of suspicion for TB in HIV-exposed/infected children.

Management

- If patient is **seriously ill** and temperature is 39^{o}C or higher, send for admission and treat empirically with ceftriaxone 50 mg/kg IM/IV BD and gentamicin 7 mg/kg IV daily. Seriously ill children should also receive supportive care including intravenous fluids, +/- oxygen, and should be monitored closely. Consider empiric treatment for malaria.
- If the patient is **not seriously ill** and no focus can be identified, empirically treat with: amoxicillin 80-100 mg/kg/day divided BD-TDS x 10 days and antipyretics.
- If the fever does not resolve and the child is well, consider fever due to HIV itself and revaluate with investigations above.

5.5 Skin and Mouth Conditions

Skin conditions are commonly the initial manifestation of HIV infection. Pruritic papular eruptions can cause significant distress to children and frequently get superinfected, prompting a caregiver to bring them for treatment. Scabies should always be ruled out in these cases and all contacts should be treated. Persistent, painful, superficial ulcers are often indicative of herpes simplex infection. Oral fungal, bacterial, or viral lesions occur in 40-50% of HIV-positive persons, often early in the course of the disease. Early recognition and treatment of these oral lesions may reduce morbidity.

A. CANDIDIASIS

Candida is the most common cause of fungal infections in HIV-infected children. Oral thrush is the most common manifestation, though oesophageal candidiasis and invasive candidiasis may also be seen. In infants under 6 months of age, mild oral candidiasis can be "normal" and not a clinical sign of advanced HIV.

History/Symptoms

- Complaints of persistent white patches in the mouth. If oesophageal, may present as refusal to feed or painful/difficult swallowing.

Physical Signs

Oropharygeal candidiasis (oral thrush)

- Creamy white curd-like mucosal patches (pseudomembranous type) in oropharynx, palate, and tonsils which can easily be scraped off and will reveal inflamed bleeding mucosa.
- Can also present as erythematous lesions (atrophic type), hypertrophic lesions (hyperplastic type), or angular cheilitis (soreness, erythema and fissuring at the corners of the mouth).

Oesophageal candidiasis

- Seen in HIV-infected children with severe immunosuppression.
- Usually presents with concomitant oropharyngeal candidiasis and refusal to feed with odynophagia (pain during swallowing), dysphagia (difficulty swallowing), and retrosternal pain. May also cause nausea and vomiting.

Oesophogeal candidiasis is a clinical stage IV condition requiring ART.

Investigations

- Oral thrush is diagnosed by its characteristic clinical features.
- Oesophageal candidiasis might only be diagnosed in the setting of oral thrush with presence of odynophagia, dysphagia and/or retrosternal pain; has a classic cobblestoning appearance on barium swallow.

Management

Oropharyngeal candidiasis

- Treat early oral thrush topically with:
    - Nystatin 1 ml in each cheek every 6h x 7-14 days (or 3 days after clinical resolution).
    - If nystatin is unavailable, consider clotrimazole 10 mg trouches or gentian violet paint q4-6h x 14 days (or 3 days after clinical resolution) for older children and adolescents. These therapies should not be swallowed.
- If patients fails topical therapy, give oral treatment as for oesopageal candidiasis.

Oesophageal candidiasis

- Fluconazole 6-10 mg/kg on first day then 3-6 mg/kg daily x 7-14 days (Annex 10).
- If fluconazole is unavailable, use ketoconazole 3-6 mg/kg OD X 7 days (max dose 800 mg/24h). NB: Ketoconazole should be avoided in patients on ART.

B. KAPOSI SARCOMA (KS)

History/Symptoms

- Persistent raised dark lesions on skin or in oropharynx. May also present with cough if pulmonary KS.

Physical Signs

- Persistent and initially flat patches with a pink or blood-bruise colour that usually develop into nodules.

Investigations

- Biopsy is confirmatory.

Management

- See **Error! Reference source not found.**10 and Mbabane Government Hospital KS protocol.

Kaposi Sarcoma is a stage IV condition requiring ART.

5.6 Neurological Manifestations

Children with HIV infection may present with neurological manifestations due to associated conditions (infections, drug side effects/interactions, malnutrition) or due to direct HIV invasion of the central nervous system (HIV encaephalopathy). The degree of immunosuppression can help to point to a probable aetiology. These neurological manifestations can have an acute, subacute, or chronic presentation. Acute or subacute fever, headache, vomiting, and meningism (neck stiffness, Kernig's and/or Brudzinski's signs) suggests bacterial meningitis and should be managed accordingly as in non-HIV infected children. Convulsions (fits or seizures) indicate irritation to the cerebral cortex seen in encaephalitis or space-occupying lesions. Delay or regression in developmental milestones generally indicates a more chronic neurological process such as HIV encaephalopathy.

A. TB MENINGITIS

Given the high HIV/TB co-infection rate, suspicion must always be maintained for TB meningitis.

History/Symptoms

- Acute to subacute onset of fever, headache, neck stiffness, and altered mental status.

Physical Signs

- Fever, altered mental status. Can present with focal neurologic signs in cases of tuberculomas.

Investigations

- Lumbar puncture demonstrating mycobacterium. In cases of focal neurologic signs, CT scan can help identify tuberculomas.

Management

- See National TB Guidelines for extrapulmonary TB treatment protocol.

B. *CRYPTOCOCCUS NEOFORMANS*

Cryptococcal infection can cause fever, pulmonary infection, chronic meningitis, disseminated disease (CNS, skin, etc.) and/or septic shock in the immunocompromised child. Cryptococcal meningitis is the most common manifestation of cryptococcosis in HIV-infected children but occurs (approximately 1-3%) less frequently than in adults.

Cryptococcal infection is a stage IV condition requiring ART.

History/Symptoms

- Subacute onset with fever, headache, and altered mental status, which evolves over several weeks.
- More common in 6-10 year old children with severe immunosuppression.

Physical Signs

- Altered mental status.
- Papilloedema.
- Focal neurological deficits or meningeal signs such as stiff neck are rare, and make diagnosis of cryptococcal meningitis less likely.
- Elevated cerebrospinal fluid (CSF) opening pressure (>20 cm H_2O).

Diagnosis

- Keep a low threshold for performing a lumbar puncture. Over 90% of children will have positive India ink stain. Half will have normal routine CSF studies (glucose, protein, cell counts). If possible, send serum and CSF for cryptococcal antigen.

Management

- Admit, stabilize, monitor
- Lumbar puncture for CSF studies, and repeat after 2 weeks.
- Repeat therapeutic lumbar punctures to control CSF pressure.
- Drug management: amphotericin B followed by fluconazole as per **Error! Reference source not found.**10.
- Initiate ART.
- Secondary prophylaxis: following completion of therapy, children should receive oral fluconazole 6mg/kg (max 200mg) daily for life, or at least until CD4/CD4% are above severe immunosuppression values for 6 months.

C. CEREBRAL TOXOPLASMOSIS

Toxoplasma gondii is a protozoal parasite known to cause toxoplasmosis encaephalitis in HIV-infected children. Since most cases are due to reactivation of latent infection, it is a more common cause of intracranial mass lesions in HIV-infected adults than children and only occurs in about 1% of HIV-infected children.

CNS toxoplasmosis is a stage IV condition requiring ART.

Symptoms and signs

- In any HIV-infected child with severe immunosuppression, any new neurologic findings are highly suggestive of toxoplasmosis: specifically partial focal seizures, eye pain, reduced vision, nausea, vomiting, headache, chorioretinitis, papilloedema, and altered mental status.

Investigations

- A presumptive diagnosis of CNS toxoplasmosis is based on clinical symptoms and serologic evidence of infection. When feasible, a computerized tomography (CT) scan of the brain should be performed, which often shows multiple, bilateral, ring-enhancing lesions especially in the basal ganglia and cerebral cortico-medullary junction.

Management

- Admit, stabilize, and monitor.
- Lumbar puncture for CSF studies and neuro-imaging, if available.
- Acute therapy and prophylaxis; see **Error! Reference source not found.**10. If mass effect, give corticosteroids.
- Initiate ART as soon as child is stable.

D. HIV ENCAEPHALOPATHY

HIV is a neurotropic virus; it crosses the blood-brain barrier through infected monocytes and infects microglial cells. The symptoms and signs of HIV encaephalopathy will vary depending on the age and developmental stage of onset. For perinatally-infected children, HIV encaephalopathy most commonly develops during the first two years of life. For this reason, all HIV-infected children under 24 months of age have a detailed developmental evaluation and periodic monitoring (every 3 months) to assess for delay or regression of milestones.

HIV encaephalopathy is a stage IV condition requiring ART.

History/Symptoms

- Common presentations include delay in achieving or loss of developmental milestones (motor or language), irritability, and poor feeding.

Physical Signs

At least one of the following, progressing over two months in the absence of another illness:

- Cognitive deficits: loss of or failure to attain developmental milestones (Annex 5) or loss of intellectual capacity.
- Microcephaly: head circumference below the 5^{th} percentile for age, or failure of head circumference to grow.
- Motor deficits: symmetrical spastic paresis with increased reflexes (pyramidal motor deficit), gait disturbance, or ataxia. Facial motor signs such as abnormal eye movements. In infants, hypotonia predominates: “floppy baby” with poor head control, needing support to sit, and with few spontaneous movements.

Investigations

- Diagnosis is made clinically. CNS imaging can help as per **Error! Reference source not found.**10.

Management

- ART reduces viral replication and reduces the risk of CNS invasion.
- Cognitive stimulation.
- Pain management and physical therapy for muscle contractions.
- Assess home environment, parental involvement, feeding difficulties, and safety issues. Provide supportive intervention.

Chapter 6 Nutrition in HIV

Nutrition plays a crucial role in child health and in HIV in particular. HIV infection increases nutrient requirements as well as impairs nutrient intake and absorption. In this way, HIV increases the risk of malnutrition. Poor nutrition also weakens the immune system and increases the risk of opportunistic infections.

Both HIV-exposed and HIV-infected children may be at increased risk of malnutrition for many reasons, including:

- Low birth weight
- Inappropriate/suboptimal infant feeding practices
- Household food insecurity
- Decreased intake due to oral diseases (e.g., thrush)
- Anorexia associated with illness
- Increased loss of nutrients because of diarrhoea and malabsorption
- Increased metabolism because of HIV infection or other infections
- Inadequate child care, if the mother is sick or deceased

Strategies to prevent malnutrition and promote good nutrition include:

- Providing prompt early treatment of common infections and opportunistic infections (e.g., thrush)
- Ensuring good health and nutritional status of women and other caregivers of infants and young children and ensuring adequate nutrient intake based on locally available foods

See Swaziland *Integrated Management of Malnutrition for Children and Adolescents* Guidelines for specific detailed strategies.

6.1 Nutritional Needs of HIV-Exposed and Infected Children

HIV-infected children have specific nutritional needs. The energy requirements of HIV-infected children with no symptoms are increased by 10 percent. During an illness without weight loss, energy requirements increase by 20 to 30 percent over the level of energy intake recommended by healthy non-HIV-infected children of the same age. When the child is both symptomatic and losing weight, energy requirements increase by 50 to 100 percent. See Annex 22 for detailed information on appropriate foods to recommend based on the child's age.

HIV infected children require calorie-dense foods due to increased metabolic demand.

6.2 Assessment of Nutritional Status

At the first and subsequent visits, measure weight, height and MUAC (mid upper arm circumference), and look for presence of oedema. Use the Weight for Height (W/H) Tables in Annex 19 to determine the percent wasting. Determine the nutritional status by using the Table 18 below. For further recommendations for children refer to the *Integrated Management of Malnutrition for Children and Adolescents* Guidelines.

Table 18. Nutritional Assessment of Children

Nutritional Status	W/H		MUAC* (6-59 mo)		Oedema	Action
Good nutritional status	>85%	and	>12.5	and	None	Age appropriate counselling
At risk	80-85%	or	12-12.5	and	None	Counsel regarding nutritional status
Moderate acute malnutrition	70-79%	or	11-11.9	and	None	Refer for out-patient therapeutic feeding (or in-patient if complications)
Severe acute Malnutrition	<70%	or	<11	or	Yes	Refer for out-patient therapeutic feeding (or in-patient if complications)
* Only W/H is used for diagnosing malnutrition in children over 5 years of age.						

6.3 Infant Feeding

Infant feeding should be discussed at each clinic visit with consideration of the infant's HIV status. Swaziland's adoption of the new recommendations from WHO for extended NVP prophylaxis (Chapter 3) to reduce the risk of HIV transmission through breastfeeding has made breastfeeding the safest option for most HIV-exposed infants. All healthcare workers should recommend and promote breastfeeding for all HIV-positive mothers to ensure HIV-free survival.

A. THE FIRST 12 MONTHS

As per the 2010 WHO Infant Feeding Guidelines, HIV-infected mothers "…should exclusively breastfeed for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life." Mixed feeding is dangerous during the first six months of life as it increases the chances of HIV transmission. Health workers should ensure that support for mothers is available to assist them in successful exclusive breastfeeding. The addition of complementary foods to breastfeeding after six months is safe and necessary for continued adequate nutrition.

B. OVER 12 MONTHS OF AGE

HIV-Negative but Exposed Children

At 12 months, in HIV negative but exposed babies, the mother and baby should be assessed and counselled regarding feeding choices. Cessation of breastfeeding should only be *considered* if the child is growing well and a nutritionally adequate and safe diet without breastmilk can be provided (Annex 21). At this point, a rapid HIV test should be conducted.

- If the rapid test is negative, breastfeeding can be stopped gradually over one month. The rapid test should then be repeated 2 months after breastfeeding cessation for a definitive diagnosis.
- If the rapid test is positive, a confirmatory DBS (DNA PCR) test should be conducted and the mother should be encouraged to continue breastfeeding with NVP prophylaxis while awaiting the result. If the DNA PCR is positive, the mother should be counselled to breastfeed as long as possible and the infant referred for ART initiation. NVP prophylaxis should be stopped.

HIV-Positive Children

Breastfeeding should be continued for as long as is feasible in HIV-positive babies. The breastmilk provides important additional protein and energy, and contains maternal antibodies that help prevent opportunistic infections.

Box 8. Summary of infant and young child feeding recommendations

Infant and Young Child Feeding Recommendations

- **Under 6 months**: Exclusive breastfeeding (only medicines can be taken, no water or other foods).
- **6-12 months**: Breastfeeding PLUS complementary feeding
- **At 12 months**: Assess nutritional status and diet and make recommendations for feeding based on infant HIV status and availability of safe and nutritious breastfeeding alternatives.
    - HIV-negative: Stop BF gradually when nutritionally adequate and safe diet is available
    - HIV-positive: Breastfeed as long as possible

C. KEEPING BREASTFEEDING SAFE

Breastfeeding can be made safer by providing ART to eligible mothers, daily NVP prophylaxis to infants whose mothers are not on ART (Chapter 3) and addressing problems of cracked nipples, mastitis, and candidiasis (in both mother and baby).

D. GOOD WEANING FOODS

The availability of high calorie, high protein food is imperative for successful weaning (Annex 22). Recommendations that can be given to families and caregivers include:

- Increasing nutrient density of foods without visibly increasing the volume of the meal by adding peanut butter, oil, skimmed milk powder, or eggs in soups or porridge.
- Providing high protein snacks between meals (e.g., boiled eggs and avocado).

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E. INDICATIONS FOR EXCLUSIVE REPLACEMENT FEEDING

Only when ALL conditions for safe and nutritious breastmilk alternatives are met can exclusive replacement feeding (ERF) be recommended. An assessment tool can be found in Annex 20. If a family meets these criteria, the following is recommended:

- For infants under 6 months of age: exclusive commercial infant formula is the only suitable replacement feed in the first 6 months of life.
- For children over 6 months of age: commercial infant formula or animal milk (boiled for infants less than 12 months) should be provided along with nutritionally rich complementary foods, for a minimum of four to five feedings per day.

F. ORPHANED INFANTS

Infants that are orphaned or separated from their mothers may be given formula feeds. Wet nursing is no longer recommended. In extreme situations, when an orphaned infant less than 6 months does not have access to breast milk or formula, using modified goat or cow's milk mixed with additional water and sugar can be used as a last resort (see Annex 23 for more information).

Chapter 7 HIV and TB Co-Treatment

The co-management of both TB and severe HIV infection in children is complicated by several factors including drug interactions, limited drug formulations, and limited data on dosing (particularly in those less than 3 years old). WHO recommends initiating ART for all patients on TB treatment who are co-infected with HIV.

TB is a Stage III or IV condition requiring initiation of ART.

7.1 Diagnosing TB

All HIV-positive children should be screened for TB at every clinical encounter. Because of the high prevalence of TB in Swaziland, and the morbidity and mortality associated with TB/HIV co-infection, a high level of suspicion should be maintained at all times. Remember that severely immunocompromised children may not show overt signs of TB infection. See Swaziland National TB Guidelines for detailed treatment information; paediatric dosing is summarized in Annex 25.

Box 9. TB Screening questionnaire

Screen all HIV-positive children for TB at every visit.

Screening questions	Yes
1. Is there a history of TB contact?	
2. Has the child had cough for 2 or more weeks?	
3. Has the child had night sweats for 2 or more weeks?	
4. Has the child lost noticeable weight in last 4 weeks?	
5. Has the child had a fever for 2 or more weeks?	

If yes

If yes

OR

If yes to 2 or more

Investigate for active TB with

- ☐ SPUTUM, for children ≥ 6 yrs
- ☐ CXR
- ☐ PPD, if available

And refer to doctor for further evaluation

7.2 When to Start ART in HIV/TB Co-Infected Children

In HIV-infected children in whom a diagnosis of TB disease has been met, initiation of TB treatment is the priority before ART initiation, to reduce the risk of severe immune reconstitution inflammatory syndrome (IRIS). IRIS should be considered especially if the CD4 count is very low at commencement of ART. The decision on when to start ART after starting TB treatment should consider:

- the child's age
- pill burden
- potential drug interactions
- overlapping toxicities
- potential for IRIS versus further progression of immune suppression.

In HIV/TB co-infected children, initiate TB treatment before ART.

All HIV-positive children diagnosed with TB should be started on ART. The results of the SAPiT trial[23] in adults suggest that ART should be initiated in all patients with TB regardless of CD4 within the first few months of TB treatment, and that waiting until the completion of TB treatment was associated with worse outcomes. In general it is safer and beneficial to start ART 2-8 weeks after starting anti-TB Treatment.

Do not delay ART in children with severe HIV disease.

7.3 ART Regimens for Children on TB Therapy

ART in the setting of TB treatment is complex. Rifampicin's metabolism via the cytochrome P450 enzyme system results in a 35% reduction in NVP levels and an 80% reduction in LPV/r levels[24,25]. Increasing the dose of either NVP or LPV/r has not been shown to reliably achieve therapeutic dosing[26,27]. For children over 3 years of age and over 10kg, use of an EFV-based ART regimen achieves viral suppression equally in patients regardless of rifampicin co-administration. However, for children under 3 years or under 10kg, options are suboptimal and include:

- Super-boosting LPV 1:1 with ritonavir - pharmacologically sound, but single-agent ritonavir is costly, famously unpalatable, and currently not widely available in Swaziland.
- Using a NVP-based regimen – doubles the risk of virologic failure in ART naïve patients on anti-TB therapy compared to those not on anti-TB therapy. However, for patients already on a NVP-based regimen who are subsequently initiated on TB therapy, reduction in NVP levels may not be as clinically significant since patients will likely have low or undetectable viral load.
- Using a triple NRTI regimen - Studies in adults show that triple NRTI-based regimens do not achieve good viral suppression in about 30% of patients[28]. No paediatric studies have been conducted.

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[23] Karim SA et. al. Timing of Initiation of Antiretroviral Drugs during Tuberculosis Therapy. NEJM 2010; 362(8): 697-706.

[24] A Randomized Trial Comparing Plasma Drug Concentrations and Efficacies between 2 Nonnucleoside Reverse-Transcriptase Inhibitor–Based Regimens in HIV-Infected Patients Receiving Rifampicin: The N2R Study. Manosuthi et al. Clin Infect Dis 2009; 48:1752–9

[25] Effect of Rifampicin on Lopinavir Pharmacokinetics in HIV-Infected Children With Tuberculosis. Ren et al. J Acquir Immune Defic Syndr 2008;47:566–569

[26] Dose adjustment of the non-nucleoside reverse transcriptase inhibitors during concurrent rifampicin-containing tuberculosis therapy: one size does not fit all.

[27] Double-dose Lopinavir/Ritonavir Provides Insufficient Lopinavir Exposure in Children Receiving Rifampicin-based Anti-TB Treatment. McIlleron et al. CROI 2009 Abstract #98

[28] Gulick RM et al, Triple-Nucleoside Regimens versus Efavirenz-Containing Regimens for the Initial Treatment of HIV-1 Infection. N Engl J Med 2004;350:1850-61.

The WHO recommends a triple NRTI regimen for children under 3 years who are NVP-exposed. For children who are placed on a NVP-based regimen, the WHO recommends using a dose of NVP at 200mg/m^2. Given the paucity of evidence supporting these WHO recommendations, and the fact that that no regimen is optimal, Swaziland will opt for a standard-dose NVP-based regimen in children under 3 years old for ease of implementation and to optimize the chance for good adherence.

Table 19. HIV/TB co-treatment ART regimens

HIV/TB co-treatment ART regimens for children who are treatment naïve or on any 1st line ART regimen	
Age < 3 years	**Age > 3 years**
AZT – 3TC – NVP*	**AZT – 3TC – EFV**
*If patient is on TB therapy and is ART naïve, NVP should be initiated at twice-daily dosing. Due to enzyme induction by rifampicin, lead-in dosing is not indicated and will increase the risk of developing NVP resistance.	

Alternative HIV/TB co-treatment ART regimen options for special situations		
Special Situation	**Alternative Regimen**	**Comments**
Currently on or qualifies for LPV/r-based 1st line regimen	May use LPV/r boosted 1:1 with ritonavir, if available	Only use if ritonavir availability can be ensured for the duration of TB treatment
Patient on 2nd line therapy	If regimen contains LPV/r, continue with 1:1 ritonavir-boosting	Consult a TB or HIV specialist if ritonavir not available
Children > 3 years already on NVP-based regimen prior to initiating TB treatment	AZT – 3TC – NVP	Studies in adults show that NVP-based regimens maintain viral suppression as well as EFV-based regimens in this situation[29]
NVP or EFV toxicity	AZT – 3TC – ABC	Immediately switch to LPV/r-based regimen when TB therapy completed
Severe anaemia (Hb < 8 g/dl)	Use d4T instead of AZT	Children with non-AZT-induced anaemia should be switched to AZT once Hb > 8.

[29]Outcomes of Nevirapine- and Efavirenz-Based Antiretroviral Therapy When Coadministered With Rifampicin-Based Antitubercular Therapy. Boulle et al. JAMA. 2008;300(5):530-539.

7.4 Monitoring Children on TB and Antiretroviral Therapy

Given the morbidity associated with TB, and the potential overlapping medication toxicities with combined TB therapy and ART (especially peripheral neuropathy and hepatitis), children on TB/HIV co-treatment need close monitoring. Weight should improve, symptoms of TB should decrease, and clinical evaluation for medication toxicities such as peripheral neuropathy and hepatitis should be conducted. Laboratory tests should be done as needed based on symptoms.

In children on HIV/TB co-treatment, monitor for medication toxicities such as peripheral neuropathy and hepatitis.

If a child does not show significant improvement within a few weeks on TB therapy, further evaluation and treatment are urgently needed. Both MDR and XDR-TB have been diagnosed in children in Swaziland and should be considered, especially in cases where the child has been in contact with an MDR/XDR-TB case, or where the TB contact has died. Other opportunistic infections should be investigated. Finally, chronic lung disease and lymphoid interstitial pneumonitis (LIP) can mimic TB and should be considered.

Poor response to TB treatment should raise suspicion for MDR-TB, other OIs, or chronic lung disease.

7.5 ART Regimens for Children Post-TB Therapy

Once TB treatment is completed, it is important to switch children to a standard ART regimen, especially given the likelihood of poor viral suppression in patients co-treated with rifampicin and NVP and in patients on triple NRTIs. If available, viral load should be checked at the end of TB therapy to determine the most appropriate post-TB ART regimen. If viral load is not available, then follow recommendations below.

Table 20. Post-TB treatment ARV Regimen Recommendations

Post-TB ARV Regimen Recommendations if VL Not Available	
Pre-TB regimen	**Post-TB regimen**
Treatment-naïve	**Continue regimen initiated during TB treatment***
NVP-based	**NVP-based**
LPV/r-based	**LPV/r-based**

*If over three years, recommend switching EFV to NVP to simplify regimen.

7.6 TB Prevention in Children

A. BCG VACCINATION

All children should be given BCG vaccination at birth per Swaziland EPI guidelines. However, HIV-infected children who missed the BCG vaccination at birth should not be given the BCG. These children are at risk of developing BCG disease.

B. ROUTINE CONTACT INVESTIGATION

Childhood contacts of adult TB cases should be investigated for TB. Such adults will continue to transmit TB to other household children unless the adult is identified and treated.

C. COUGH ETIQUETTE FOR BREASTFEEDING MOTHERS

Cough etiquette is essential for breast feed mothers to prevent transmission of TB to her infant. Masks can be worn by the mothers while breastfeeding, and are especially important if the mother has MDR-TB.

Breastfeeding mothers with active TB should wear a mask while breastfeeding.

D. INH PREVENTIVE THERAPY (IPT)

Isoniazid (INH) preventive therapy (IPT) is recommended for all HIV-infected patients with latent TB infection. The high prevalence of TB in Swaziland puts all patients at risk of latent TB and the potential to develop active TB disease. Active TB disease must be ruled out prior to IPT. A screening algorithm to identify patients that qualify for IPT is provided in Annex 24. If a child screens positive for TB, a thorough investigation should be conducted. If TB is diagnosed, TB therapy should be initiated per the Swaziland National TB Guidelines. Annex 25 provides a dosing summary for standard initial (Categories III and I) TB treatment.

If no signs or symptoms of TB are present, IPT should be given for 6 months' duration at a dose of 10mg/kg daily (Annex 24). Pyridoxine at 1-2mg/kg daily should be given to prevent side effects. Ideally, adherence to IPT should be monitored. IPT should be repeated at least every three years. However if a child has been in the presence of a known TB contact, IPT should be repeated sooner. IPT should be given to a child who has previously been treated for active TB if a new known contact is identified or it has been three years since the completion of anti-TB treatment.

For ART-eligible children who screen negative for active TB, it is recommended to delay IPT until 6 months after the initiation of ART. This allows time to watch for TB IRIS and also minimizes pill burden and confusion at the start of ART. A child who develops TB IRIS while receiving IPT should be switched to standard TB treatment.

Box. 10 Summary IPT Recommendations for HIV infected children

IPT Recommendations for HIV Infected Children

All HIV infected children who screen negative for TB should be initiated on INH prophylaxis for 6 months.

For ART-eligible children, IPT should be initiated 6 months after ART initiation.

Dosing of IPT:

- **INH 10 mg/kg daily (max 300mg)**
- **Pyridoxine 1-2mg/kg daily (max 100mg)**

Chapter 8 Care of HIV-Infected Adolescents

Adolescents are a special population with unique challenges. Adolescents may have been infected with HIV either at birth or later in life. They are not "older children" nor are they "little adults". In fact, adolescence is a period of transitioning from childhood to adulthood, with many physical, mental, and emotional changes. These changes can affect an adolescent's wellbeing and may influence the dynamic between the adolescent and the health care system, making management of care challenging.

The most critical aspect of appropriate care for HIV-infected adolescents is monitoring their psychosocial health.

The most critical aspect of providing appropriate care to HIV-infected adolescents is closely monitoring their psychosocial health. Even in adolescents living with HIV, accidents from high-risk behaviour, suicide, and homicide are still preventable leading causes of morbidity and mortality. A brief, confidential conversation with an adolescent patient is often all that is required to prevent these issues.

Most HIV-infected adolescents have special psychosocial issues such as:

- Denial and fear related to HIV diagnosis
- Misunderstandings related to their status and health needs
- Lack of belief in the efficacy of ARVs
- Distrust of family, practitioners, and the healthcare system
- Low self-esteem and unstructured, chaotic lifestyles
- Limited family and social support

These factors may affect adherence and can also lead to risk-taking behaviours that can place them in vulnerable situations or possibly expose others to harm, including HIV-infection. **HCWs should explore with the adolescent issues of sexuality, safe sex, substance abuse, barriers to adherence, and community support**. Risk-taking behaviours need to be assessed and addressed on an ongoing basis by health care providers (See **Error! Reference source not found.**).

Positive adult guidance is always encouraged. Many adolescents are confronted with issues of peer pressure and this can lead to making suboptimal choices. Those adolescents with lack of positive adult influence are especially at risk. Adult-supervised adolescent peer support groups provide a safe place for adolescents to share their status, discuss common concerns, develop self-esteem, and promote positive living.

Positive adult guidance assists in reducing risky behaviour in adolescents.

8.1 Counselling for the Adolescent Patient

A. INTERACTING WITH ADOLESCENT PATIENTS

Adolescent patients should be given the opportunity to discuss their health in a private, confidential manner without the presence of a caregiver, at every visit. Awareness of the stages of adolescence may assist HCWs to interact with their adolescent clients in a more appropriate manner. There are three stages of adolescence with varied thinking processes, behaviours, and social relationships that should be considered. It should be noted that the developmental stages may be significantly delayed in those adolescents who were infected at birth versus those infected later in life.

Table 21 Adolescent Developmental Stages

Age	Thought Process	Behaviour	Social Relationships
10-13	Very concrete	Impulsive	Self-image is confused Relation with elders shifting toward peers Peers increasingly important
14-16	Early abstract reasoning, emotional immaturity	Impulsive, withdrawn in social situations	Highly self-conscious Less regard for authority figures Peer groups highly valued
17-21	Mature cognitive ability with abstract reasoning and awareness of consequences	Deliberate, well thought out	Established self-image Comfortable with adults and peers Individual relationships valued over peer groups

B. CONSENT AND ASSENT FOR ADOLESCENTS

Anyone age 16 years or older is able to give full informed consent. Consent can be given by parents, guardians, caregivers, or health or social workers. Although children may not give informed consent for testing, their agreement (assent) to testing should be sought through age-appropriate counselling.

Age of consent is 16 years

Children considered premature adults may also give their own consent

Parents, guardians, caregivers, health care workers, or social workers may give consent for a child under 16.

Children under the age of 16 may provide their own informed consent for HIV testing if they are considered to be a premature adult (pregnant, being treated for a sexually transmitted infection, accessing family planning services, and/or are sexually active). In situations where adolescents present to health care or testing facilities on their own or as the primary caregiver for a younger sibling, they should be asked to identify a guardian, caregiver, or health or social worker to consent on their behalf. The process of obtaining consent for HIV testing should follow the same procedure as for other medical procedures and diagnostic tests, always keeping in mind the best interest of the child.

Please see Chapter 2 and the *Swaziland National Guidelines on HIV Testing and Counselling* for more details on ethical consent for HTC.

C. ADOLESCENTS AND DISCLOSURE

Disclosing to an Adolescent

Adolescents must know their HIV status. Benefits include improved self-esteem, autonomy, empowerment, and psychological adjustment. The process of disclosure promotes honesty and trust within the adolescent-adult relationship and facilitates dialogue about chronic treatment and positive prevention.

Adolescents must know their HIV status.

More often than not, adolescents are aware of their status well before official disclosure takes place. When disclosing to an adolescent, the HCWs should consider the patient's social, family, and medical histories and take into account the age, mode of transmission, psychosocial maturity, prior knowledge, and past experiences.

Adolescents Disclosing to Others

Many adolescents fear disclosure.

Many adolescents fear disclosure. The adolescent should be counselled on the pros and cons of disclosing to friends, family, and at school and community. It is critical that normality and positive living are emphasized when dealing with this age group. It is also important that responsibility to one's sexual partners is discussed, with consideration to the fact that disclosure is unlikely with casual sex encounters. Disclosure can facilitate improved access to care and support, and can encourage an increased sense of control over one's life. HCWs should assist patients with the process of disclosure to their families and communities by providing strategies and encouragement. See Chapter 9.4 for more details on disclosure.

Disclosure can improve access to care and increase the sense of control over one's life.

D. ADHERENCE PREPARATION

As for any patient, adolescents need comprehensive preparation for ART adherence (see Chapter 4 and Annex 11). In addition, adolescents should:

- be fully disclosed to,
- participate in their treatment plan, and
- be empowered to take responsibility over their health and life choices.

It is important that adolescents identify a treatment supporter before initiation of ART. While family support and involvement is strongly encouraged, adolescents are developing independence and a peer, teacher, or other community member may be an appropriate treatment supporter.

E. SUPPORTING ADHERENCE

There are factors that compromise adherence in adolescents such as side effects, adverse events, peer pressure, lack of disclosure, drug fatigue and waning adult supervision. Assessment of adherence at each visit provides an opportunity to catch these problems early, intervene, and minimize the risk of treatment failure. HCWs' attitudes towards adolescents on ART should be supportive and non-judgmental, giving them the permission to disclose challenges and barriers to adherence without intimidation and fear. With information, HCWs can form an alliance with adolescents to help them handle challenges that may arise.

Adherence must be assessed at every visit.

Treatment supporters, caregivers, and supportive family members who are aware of the adolescent's HIV status can be called on if the adolescent's adherence is repeatedly poor. Adolescents should be linked to a regular ART support group where issues that are relevant to their age group are discussed and support is given. Home visits can be done to ensure that the patient adheres well to ART, and to address challenges with insight into the home environment.

F. SEXUAL AND REPRODUCTIVE HEALTH ISSUES

Adolescents are exploring their sexuality, and often HCWs find this difficult to address. According the Swaziland Demographic and Health Survey, 39% of girls have given birth before they turn 20, and only 29% of sexually active girls ages 15-19 reported ever using contraception. These circumstances highlight the importance of discussing sexual and reproductive health issues with all HIV-infected adolescents including:

- Responsibility and disclosure to sexual partners
- Dating and marriage
- Positive prevention behaviours, including abstinence, mutual faithfulness, and condom use
- STI risks, prevention, and treatment
- Family planning and prevention of unwanted pregnancies

Adolescents face special needs when choosing a contraceptive method. Social and behavioural issues are important considerations. Sporadic patterns of intercourse and the

need to conceal sexual activity make a daily regimen less appropriate. Proper education and counselling both before and at the time of method selection can help them address their specific concerns and make informed and voluntary decisions.

Discussions about sexual and reproductive health, including the provision of family planning, should be integrated into the comprehensive care of adolescents.

Adolescents are also thinking about future possibilities of starting a family. Fears about being accepted, having safe long-term relationships, and being judged for wanting a family further complicate this issue. It is important to address these concerns, provide reassurance, and refer for ongoing counselling or peer support if needed.

8.2 Medical Management of HIV-Infected Adolescents

Adolescents who obtained HIV from vertical transmission often present with clinical manifestations of chronic infection. Adolescents who have obtained the virus from horizontal transmission can present with symptoms of acute HIV, in the early stages of the disease, or with chronic manifestations.

A. ART REGIMEN

ART Regimens for Adolescents
Less than 12 years old: use Paediatric Guidelines
12 years and above: use Adult & Adolescent Guidelines

EFV should be used with caution in adolescent girls at risk of pregnancy (i.e., sexually active and not using adequate contraception) or in the first trimester of pregnancy. Simplification of treatment regimens and anticipated long-term adherence are further important considerations. See Chapter 4 for first- and second-line paediatric options and the *Adult and Adolescent Comprehensive Care Package* for medications and dosage for children over 12 years of age.

B. DISCONTINUATION

Non-adherence is a major challenge in adolescent care. Due to their reliance on adult caregivers and the unique challenges of adolescence, it is sometimes necessary to temporarily discontinue ART in paediatric and adolescent patients who are unable to take their medications reliably. Although interrupted therapy does carry an increased risk of morbidity and mortality, this step may be necessary in some circumstances in order to preserve future treatment options.

Discontinuation of ART should never be considered a punitive measure, nor should it be presented as such.

The clinician must carefully and sympathetically explain to the patient and family the reasons for temporary treatment discontinuation. At the time of discontinuation, a plan for preparing the patient to safely restart therapy should be formulated and implemented. A comprehensive evaluation of the factors leading to non-adherence must be undertaken, and all available resources marshalled to address those factors. These patients should also be scheduled frequently for clinical monitoring and counselling in order to determine when ART can be safely restarted. Weekly meetings that gain the trust of the adolescent patient can be used to identify barriers to good adherence. CTX and multivitamins can help preserve the patient's health, and should also be used to re-establish the habit of good medication adherence, which can be monitored with CTX and multivitamin pill counts at each visit. See Chapter 9 for further recommendations.

Chapter 9 Psychosocial Care and Counselling

9.1 The Importance of Psychosocial Support

Both children and their caregivers have psychosocial needs which must be identified and addressed as integral components of the holistic approach to HIV care and treatment. Psychosocial support optimizes the psychological, social, emotional, and mental well-being of people. The focus extends from the individual to the households, families, and community. With regards to children, it is important that psychosocial support is facilitated in an age- and developmentally appropriate manner.

9.2 Developmentally Appropriate Counselling

All HIV-infected and affected children need counselling. Counselling is intended to help the child and family cope with the emotions and challenges they experience as a result of HIV infection in the family. Such counselling helps HIV-infected and affected children adopt a positive living attitude. This in turn can help them improve their quality of life, and adhere better to a treatment regimen.

Children's understanding of the world, thought processes, and interactions with others change dramatically with age and development. They are astute observers who recognize when something unique is happening to them. It is crucial to counsel even very young children about their situations so they obtain accurate information about diagnosis and are active participants in their care and treatment.

Counselling should be provided to all children using age and developmentally appropriate messages.

Whether counselling about testing, disclosing results, or discussing adherence, the following general principles should be followed:

- Make the child feel comfortable and safe: Greet him/her with a smile and introduce oneself
- Determine whether or not the child should be counselled individually or with the caregiver present (it may be appropriate to counsel both individually and jointly)
- Use age- and developmentally appropriate language and concepts (Annex 2)
- Assess the child's knowledge and understanding of HIV (including modes of transmission); fill in gaps and correct myths and misconceptions
- Take into consideration the child's experience with other illnesses and treatments
- Evaluate family structure and family dynamics
- Explain the benefits of early awareness and treatment of HIV infection in the child's life and for the family
- Provide a forum for the child and/or caregiver to ask questions
- Obtain the child's assent for the procedure or treatment

9.3 Pre-Test Information and Post-Test Counselling

Pre-test information and post-test counselling messages as well as issues related to consent are detailed in the *Swaziland National Guidelines on HIV Testing and Counselling*. A summary of age-appropriate counselling messages and consent guidelines can be found in these guidelines in Annex 2 and Chapter 2.3, respectively.

9.4 Disclosure of HIV Status

More often than not, children are aware of their status well before disclosure takes place.

Disclosure to a child may happen immediately after testing, or may happen during the course of care and treatment. More often than not, children are aware of their status well before disclosure takes place. Although disclosure to children can be difficult, it is especially beneficial.

Table 22. Benefits of disclosure and consequences of non-disclosure

Benefits of Disclosure	Consequences of Non-Disclosure
• Promotes honesty and trust within the child-caregiver relationship. • Gives children permission to openly ask questions about their status. • Provides caregivers and healthcare workers an opportunity to promote positive living and educate about positive prevention. • Enables children be involved in their treatment plans, facilitating greater control over their health. • Facilitates autonomy, empowerment, self esteem, and an improved psychological adjustment.	• Refusal of treatment. • Defaulting on treatment with subsequent viral resistance. • Acquisition of misinformation from non-professional sources. • Development of dishonesty, mistrust, and betrayal in the child-caregiver relationship. • Keeping of secrets provokes anxiety and distress in the caregiver which is transferred onto children.

A. WHO SHOULD DISCLOSE TO THE CHILD

Either the HCW or the caregiver can disclose the HIV status to the child. Many caregivers fear disclosing to children and will need to be counselled, encouraged, and supported in doing this. Regardless of who does the disclosing, the caregiver should be in agreement with the disclosure plan. In the case of an adolescent, a HCW may disclose independently if the adolescent qualifies to provide his/her own consent for testing, care, and treatment under the legal considerations detailed in Chapter 2.3.

Parents should be supported in disclosing the child's HIV status to the child.

B. HOW SHOULD DISCLOSURE BE DONE

Disclosure to children is often a process conducted over time and must take into consideration age, psychosocial maturity, level of development, and clinical context (Chapter 9.2). It should be done in an honest, empathetic, and insightful manner, validating the child's needs, feelings, and responses. Further, the child should be given positive regard and feedback at all times. Assure children they are loved unconditionally and will be cared for and supported throughout their lives. Emphasize that having HIV is not their fault; neither is it a punishment for anything they have done. Where children are unable to express themselves verbally, alternative methods of communication may be used, such as storytelling, drawing, music, journals, and drama.

Disclosure to children is often a process conducted over time and based on age and maturity level.

C. AGE APPROPRIATE DISCLOSURE MESSAGES

See Annex 2 for age-specific messages HCWs and caregivers can give to children regarding disclosure of HIV status.

D. FOLLOW-UP AFTER DISCLOSURE

Once disclosure has taken place, it is crucial that HCWs help the family/caregivers plan for the future. This assistance includes:

- Ensuring consistent clinical care and treatment services
- Monitoring the child's behaviour to determine ongoing counselling needs
- Attachment to community affiliates such as support groups, rural health motivators, community leaders, traditional healers, and community-based organizations for additional ongoing support

Where feasible, community organizations and groups should receive training on age-and developmentally appropriate counselling and support services.

E. DISCLOSING TO OTHERS

Talking to children and adolescents about disclosing to others is an important aspect of paediatric HIV care. HCWs should guide caregivers to talk with their children about who is safe to receive disclosure. Further, children should be told that they do not have to share their status unless they want to do so.

Adolescents may choose to independently disclose to others, and should be encouraged to share their status with partners and family members. Sharing their status will help them develop self-esteem while simultaneously promoting responsible positive living. HCWs and support groups can assist adolescents in disclosing their status by asking about when and how they will disclose, the reactions they anticipate, and ways to respond to those reactions. See Chapter 8 for more information on disclosure for adolescents.

9.5 Adherence Support

Ongoing adherence is very important in an HIV-infected child. Adherence tends to wane over time. Further, because children often have multiple caregivers and/or the situation with the same caregiver may change, adherence can be inconsistent. For these reasons, efforts should be made to conduct adherence monitoring and counselling at every client contact so interventions can be made early. This helps keep children on first-line treatment for as long as possible.

Conduct adherence monitoring and counselling at every visit.

Methods to monitor and enhance adherence to treatment include:

- Requesting patients to bring their medication to every visit
- Asking caregivers how they are dosing the medication
- Checking adherence by pill counting and/or measuring syrups
- Inquiring about side effects
- Identifying social barriers to adherence (e.g., stigma, family conflicts, finances)

If a problem is identified in any of the above areas, counselling to address challenges or barriers should be provided.

Box 11. Strategies to promote adherence

Strategies to Promote Adherence

- **Confirm that child has been disclosed to**
- **Involve child in treatment plan**
- **Increase family involvement**
- **Provide pill box**
- **Simplify regimen**
- **Adjust pill-taking time to better fit daily schedule**
- **Encourage child/adolescent to attend support group**
- **Refer for peer-to-peer counselling**

9.6 Special Populations

A. ORPHANED AND VULNERABLE CHILDREN (OVCS)

OVCs are at special risk of HIV infection. HCWs need to remember that OVCs' welfare and immediate needs are compromised. Due to HIV, they often experience multiple loss, economic hardship, illness, interrupted education, malnutrition, and loss of property and inheritance. Where possible, strengthen community support structures to best assist and support OVCs to stay in their communities. For children in orphanages, the family-based model is preferred to institutionalization. House 'mothers', house 'fathers', and house 'aunties' have the responsibility to consent for, disclose to, and provide treatment support for the children they look after.

B. CHILD-HEADED HOUSEHOLDS

In the absence of a treatment supporter, senior siblings can be empowered to take responsibility for the care of their younger siblings.

C. CHILDREN WITH DISABILITIES (DEVELOPMENTALLY DELAYED/MENTALLY CHALLENGED)

When a child is unable to participate in the treatment plan due to disabilities, the caregiver should be counselled on ART, supported, and empowered to assist that child as best as possible.

D. CHILDREN EXPERIENCING TRAUMA (I.E., RAPE, ABUSE, NEGLECT, LOSS)

HCWs must be aware of local organizations and structures that can evaluate and support children who have experienced trauma. Referral is crucial in these circumstances to assist the child in dealing with the traumatic event and moving forward toward a productive and healthy life. Where indicated, post-exposure prophylaxis should be provided per the Swaziland National Post-Exposure Prophylaxis (PEP) Guidelines.

E. CHILDREN EXPERIENCING GRIEF AND LOSS

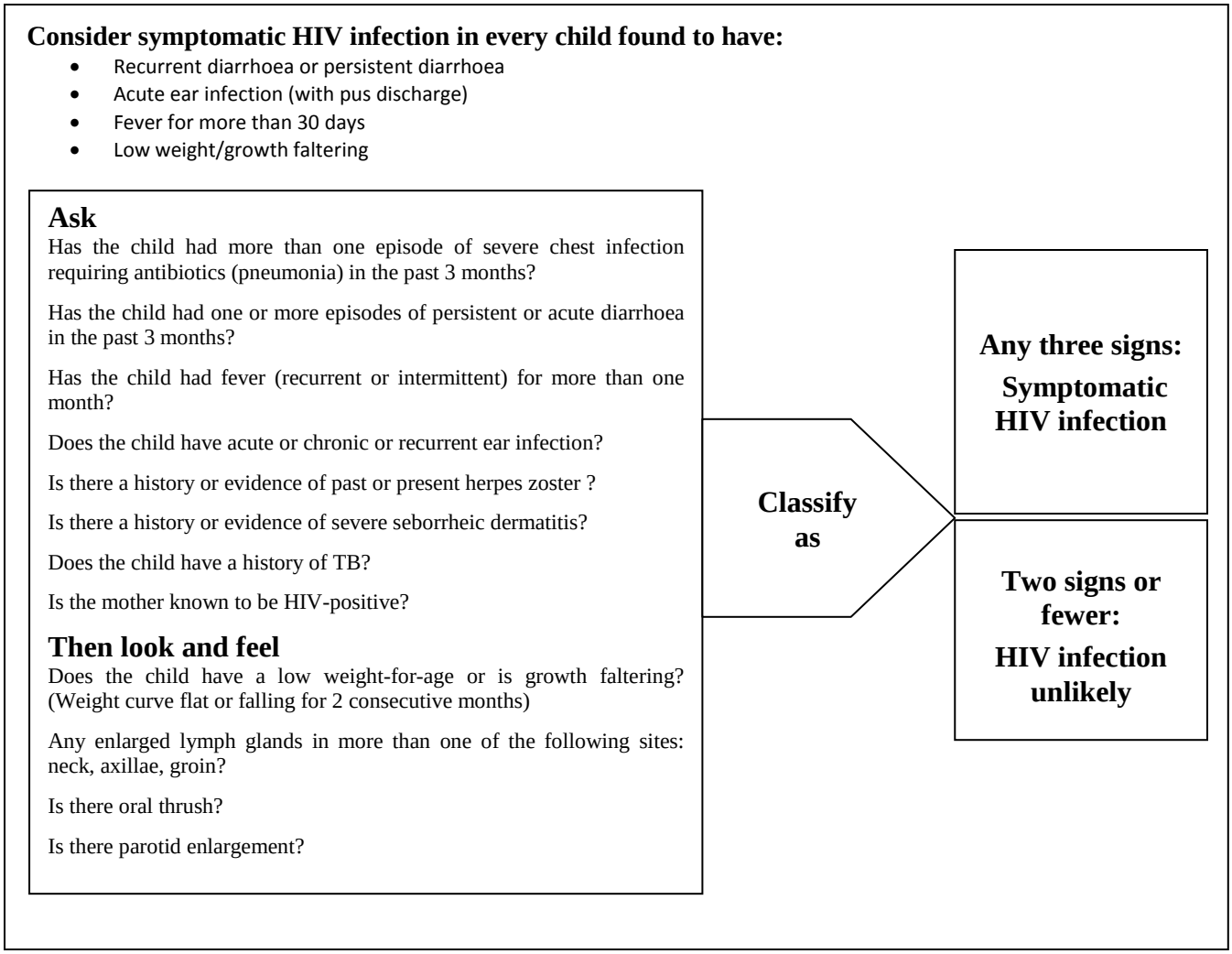
HCWs should be sensitive to the fact that many children receiving care will have lost one or both parents to HIV, and are grieving. Where possible, the HCW should link these children and caregivers to community structures what can provide ongoing support through the grieving process.

Chapter 10 Monitoring and Evaluation

TO BE WRITTEN

Annex 1 IMCI Assessment for Symptomatic HIV Infection in Children

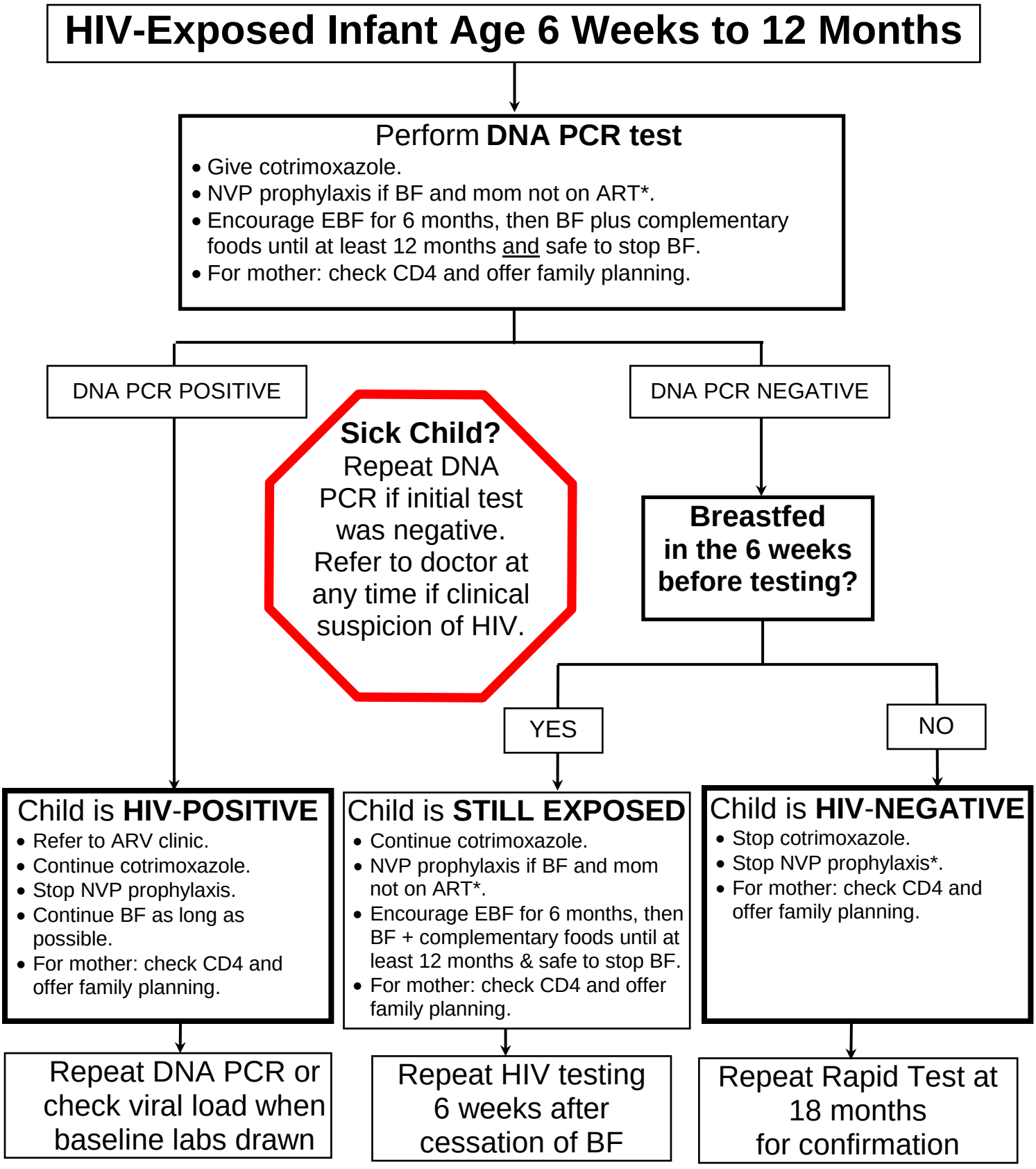
IMCI guidelines can be used to identify children with possible HIV infection, start them on cotrimoxazole prophylaxis, and arrange for HIV testing. If identified using the IMCI algorithm below, these children can be further assessed, staged, and provided with appropriate treatment and care.



Annex 2 Age-Appropriate Counselling Considerations and Messages

Age	Cognitive and behavioural development	Special considerations	Counselling messages	Counselling Tools
Under 18m	• Completely reliant on caregiver. • Crucial time for brain development.	• Many exposed infants will be healthy at time of testing. • Caregivers often do not recognize the importance of prophylaxis and early intervention.	• Cotrimoxazole & NVP prophylaxis. • Safe breastfeeding practices and appropriate complementary foods. • Timely CD4 monitoring, ART initiation and follow-up for mother. • Importance of and timeframe to collect results, retest, follow-up. • Positive infants who initiate ART before getting sick have a 75% decreased risk of dying.	• N/A
18 months to 5 years	• Moving from focus on self to attention to others. • Speaking directly and honestly. • Imagination → making up rationale for events. • Asking many "why" questions.	• Counsel child and caregiver together. • Disclosure amongst family important to health and successful treatment of child.	• HIV = 'shishi.' • Soldiers protect body. • Shishi can destroy the soldiers. • Medicines make shishi sleep. • When shishi sleeps, you stay strong and can play with friends.	• Dolls • Toys
6-12 years	• Developing logical thinking. • More interest in peer acceptance. • Often blame selves for events that happen. • Very sensitive.	• Usually provide some counselling to child independent of caregiver. • Decisions about what information to tell a child should be made in conjunction with the caregiver. • Disclosure is most often a stepwise process.	• HIV = 'shishi' in body called virus. • Virus lives in body, will be there forever, is called HIV. • Soldiers in body fight off germs (diarrhoea, flu). • HIV can destroy the soldiers. • Medicines make HIV sleep so soldiers fight to keep you strong. • You cannot get HIV by touching, hugging, being in the same school.	• Drawing • Toys • Stories
13-18 years	• Abstract thinking and deductive reasoning → complex questions. • Transitioning to adult; still feeling like a child. • Often communicating less with others. • Desiring to conform with peers. • Frequent family conflict.	• Consider implications of test results on self-image, relationships, goals. • Follow-up counselling and referral to peer support groups important. • Disclosure is recommended and highly beneficial.	• HIV should definitely be named. • Listen to adolescent's concerns. • Focus on risks. • Reassure that one can live a normal life. • Clarify misconceptions. • Address sexuality issues.	• Drawing • Discussion

Annex 3 Early Infant Diagnosis Algorithms



*NVP prophylaxis should be stopped 1 week after BF cessation

HIV Exposed Child Age 12 to 18 Months

Perform **Rapid Test "A"**

Rapid test "A" POSITIVE

Perform **DNA PCR** test
- Check CD4; Refer to ARV clinic†.
- Cont BF and reassess when DNA PCR result returns.
- Give cotrimoxazole.
- Cont NVP prophylaxis if BF and mom not on ART*.

DNA PCR POSITIVE

DNA PCR NEGATIVE

Breastfed in the 6 weeks before testing?

YES

NO

Child is **HIV-POSITIVE**
- Refer to ARV clinic.
- Continue cotrimoxazole.
- Stop NVP prophylaxis.
- Continue BF as long as possible.
- For mother: Check CD4 and offer family planning.

Repeat DNA PCR or check viral load when baseline labs drawn

Child is **STILL EXPOSED**
- Continue cotrimoxazole.
- NVP prophylaxis if BF and mom not on ART*.
- Encourage BF and complementary foods until safe to stop BF.
- For mother: Check CD4 and offer family planning.

Repeat Rapid Test 2 months after cessation of BF

Sick Child?
Repeat Rapid Test and DNA PCR if initial test was negative. Refer to doctor at any time if clinical suspicion of HIV.

Rapid Test "A" NEGATIVE

Breastfed in the 2 months before testing?

YES

NO

Child is **HIV-NEGATIVE**
- Stop cotrimoxazole.
- Stop NVP prophylaxis*.
- For mother: Check CD4 and offer family planning.

Repeat Rapid Test at 18 months for confirmation

† While awaiting DNA PCR results, immediate referral to ARV clinic is recommended due to a high likelihood of true infection.

* NVP prophylaxis should be stopped 1 week after BF cessation.

HIV Exposed Child Age 18 Months or Older

Perform **Rapid Test "A"**

Rapid Test "A" POSITIVE

Perform **Rapid Test "B"**

Rapid Test "B" POSITIVE

Rapid Test "B" NEGATIVE

INCONCLUSIVE Result

- Continue cotrimoxazole.
- Continue NVP prophylaxis if BF and mom not on ART*.
- Send blood sample to national lab as tie breaker
- For Mother: Check CD4 and offer for family planning.

Sick Child? Repeat Rapid Test if initial test was negative. Refer to doctor at any time if clinical suspicion of HIV.

Rapid Test "B" NEGATIVE

Breastfed in the 2 months before testing?

YES

NO

Child is **HIV-POSITIVE**

- Refer to ARV clinic.
- Continue cotrimoxazole.
- Stop NVP.
- Continue BF as long as possible.
- For mother: Check CD4 and offer for family planning.

Child is **STILL EXPOSED**

- Continue cotrimoxazole.
- Continue NVP prophylaxis if BF and mother not on ART*.
- Encourage BF and complementary foods until safe to stop BF.
- For mother: Check CD4 and offer family planning.

Repeat Rapid Testing
2 months after cessation of BF.

Child is **HIV-NEGATIVE**

- Stop cotrimoxazole.
- Stop NVP prophylaxis*.
- For mother: Check CD4 and offer for family planning.

* NVP prophylaxis should be stopped 1 week after BF cessation.

Annex 4 Routine Care for HIV-Exposed Infants and Children

Service	Comments	Birth	6 weeks	10 weeks	14 weeks	6 months	9 months	12 months	18 months
Immunizations	Ensure immunizations are up to date	BCG; OPV 0	DPT/HBV1; OPV1	DPT/HBV2; OPV2	DPT/HBV3; OPV3	Vitamin A	Measles	Vitamin A Albendazole	OPV 4; Measles Vitamin A Albendazole
Growth monitoring	Underweight (girls)	< 2.5kg	< 4.0kg	≤ 4.5kg	≤ 5.0kg	≤ 5.5kg	≤ 6.5kg	≤ 7.0kg	≤ 8.0kg
	Underweight (boys)	< 2.5kg	< 4.5kg	≤ 5.0kg	≤ 5.5kg	< 6.5kg	< 7.0kg	< 7.5kg	<8.5kg
Clinical assessment for HIV		Evidence of HIV is not usually present	Early evidence of poor growth or infection	Oral thrush after this age is suggestive of HIV	Weight loss; pneumonia; oral thrush	Weight loss; pneumonia; oral thrush	Weight loss; pneumonia; oral thrush; diarrhoea	Weight loss; pneumonia; oral thrush; diarrhoea	Weight loss; pneumonia; oral thrush; diarrhoea
Developmental assessment	Delay may be present if child is NOT…..	N/A	Lifting head while prone	Smiling	Controlling head	Rolling over	Sitting	Pulling to stand	Walking
Prophylaxis	**NVP** - Stop 1w after stopping breastfeeding	1ml OD if <2.5kg **or** 1.5ml OD if 2.5kg or greater	2ml OD Stop NVP if not breastfeeding or mom on ART	2ml OD Stop NVP if not breastfeeding or mom on ART	2ml OD Stop NVP if not breastfeeding or mom on ART	3ml OD Stop NVP if not breastfeeding or mom on ART	4ml OD Stop NVP if not breastfeeding or mom on ART	4ml OD Stop NVP if not breastfeeding or mom on ART	4ml OD Stop NVP if not breastfeeding or mom on ART
	CTX -Stop if definitively HIV negative with no further exposure	N/A	2.5ml OD	2.5ml OD	2.5ml OD	5ml OD	5ml OD	5ml OD	5ml OD
	INH - Give wt based dose for 6m if household TB contact		Assess for household TB contact & rule out active TB	Assess for household TB contact & rule out active TB	Assess for household TB contact & rule out active TB	Assess for household TB contact & rule out active TB	Assess for household TB contact & rule out active TB	Assess for household TB contact & rule out active TB	Assess for household TB contact & rule out active TB
HIV testing	Repeat HIV test 6 weeks after stopping breastfeeding	N/A	Do 1st DBS (DNA PCR)	Give 1st DNA PCR result.	Ensure 1st PCR has been done and result given	Ensure 1st PCR has been done and result given	Ensure 1st PCR has been done and result given	Rapid test if considering stopping BF; Repeat rapid test 6w after stopping BF	Do rapid test to confirm HIV status if previously tested negative
Feeding advice	Breastfeeding is recommended for all infants	Recommend EBF No mixed feeding	Recommend EBF. No mixed feeding	Recommend EBF. No mixed feeding	Recommend EBF. No mixed feeding	Start complimentary feeding	Complimentary feeding	May stop BF if safe & there is nutritional alternative	May stop BF if safe & there is nutritional alternative

Annex 5 Rapid Paediatric Developmental Assessment

Developmental abnormalities are common in HIV-infected children and can appear as developmental delays, cognitive deficits, behavioural/psychiatric problems, or poor school performance. Assess development through behavioural observation of the child and by asking about developmental milestones.

Age-based Normal Development and Red Flags for Developmental Delay		
Age	**Normal Milestones**	**Red Flags**
One Month	• Lift head in prone position • Facial response to sound • Stare at face • Reflexes - doll's eye, asymmetric tonic neck, Moro (startle), grasp	Inability to: • Move all extremities equally • Lift head while prone • Vocalize/respond to sound • Stare at face
Two Months	• Follow objects past midline • Lift head while prone to 45° • Coo, vowel sounds • Smile	Inability to: • Track to midline • Move all extremities equally & lift head • Vocalize/respond to sound • Stare at face
Three Months	• Follow objects 180 degrees • Head control while sitting • Coo, laugh • Smile	Inability to: • Track past midline • Grasp and hold objects • Lift head to 45 degrees • Vocalize/respond to sound • Smile responsively
Four Months	• Hands open, bring objects to mouth • Head steady • Turn toward voice • Roll to supine • Coo, laugh, squeal • Smile spontaneously	Inability to: • Control head while sitting • Push down with legs when feet are placed on a firm surface • Grasp/reach for object, bring object to mouth • Laugh/smile responsively Fisting Persistence of palmar grasp reflex
Six Months	• Intentional palmar grasp of objects • Sit independently • Stand with hands held • Babble consonant sounds • Reach for toys • Recognize strangers	Inability to: • Reach for toy • Roll over • Turn toward sound • Work for toy Presence of any neonatal reflex
Nine Months	• Pincer grasp of objects • Pull to stand • Mama, dada (non-specific) • Wave bye • Feed self	Inability to: • Stand while holding support, sit without support • Rake small object • Imitate speech sounds • Work for toy
Twelve Months	• Turn pages of book • Stand independently • Walk with one hand held • 2-4 words • Follow commands	Inability to: • Pull to stand • Bang two objects • Mama, dada (non-specific)

Annex 6 Prophylaxis Dosing for Exposed Infants: Nevirapine, Cotrimoxazole, and Isoniazid

NEVIRAPINE: All HIV-exposed infants should be started on NVP from birth, according to birth weight. Once above 2.5kg, dosing is based on age.

Infant age	Nevirapine (10mg/ml) once daily dosing	
Birth - 6 Weeks		
• Birth weight 500 - 999 grams	3mg	0.3 ml
• Birth weight 1,000 -1,499 grams	6mg	0.6 ml
• Birth weight 1,500 - 2,000 grams	8mg	0.8 ml
• Birth weight 2,000 - 2,499 grams	10mg	1 ml
• Birth weight ≥2,500 grams	15mg	1.5 ml
≥ 6 Weeks - 6 Months	20mg	2 ml
≥ 6 Months - 9 Months	30mg	3 ml
≥ 9 Months - End of Breastfeeding	40mg	4 ml

Adapted from: *Mirochnick M. et al 2006*

CO-TRIMOXAZOLE: All HIV-exposed infants should be started on CTX at 6 weeks. Dosing is based on weight or age.

		Co-trimoxazole Formulation and Dose				
Weight (kg)	**Age**	**Oral suspension** 200/40 per 5 ml	**OR**	**Paediatric tablet** 100/20	**OR**	**Single strength tablet*** 400/80
≤5 kg	< 6 months	2.5 ml		1		¼
5-15 kg	6 months – 5 years	5 ml		2		½

**Split single strength tablets into quarters only if syrups or paediatric tablets are not available*

ISONIAZID: Infants exposed to household TB contacts should receive INH for 6 months. Dosing is based on weight.

	Daily Isoniazid Dose for 6 Months	
Weight (kg)	**Dose (10mg/kg)**	**Number of 100mg INH tablets**
<5	50mg	½
5.1 – 9.9	100mg	1
10 – 13.9	150mg	1½

Annex 7 Extended Nevirapine (NVP) and Cotrimoxazole (CTX) Prophylaxis Dispensing Aid

VISIT	NEVIRAPINE			COTRIMOXAZOLE	
	SYRUP ML/DAY	BOTTLES	5 ML SYRINGE with CLIP	ONCE DAILY: ML SYRUP or 120mg TABS	BOTTLES or 120mg TABS
ANC	1.5 ml	1 x 25 ml	1.5 ml clip	N/A	N/A
Labour and Delivery	If BW < 2.5kg 1 ml	3 x 25 ml	1 ml clip	N/A	N/A
	If BW ≥ 2.5kg 1.5 ml	3 x 25 ml	1.5 ml clip	N/A	N/A
Postnatal visit (if home delivery)	Follow Labour and Delivery schedule			N/A	N/A
6 Week Visit	2 ml	3 x 25 ml	2 ml clip	2.5 ml 1 tab	1 x 100ml 30 tabs
10 Week Visit	2 ml	3 x 25 ml	2 ml clip	2.5 ml 1 tab	1 x 100ml 30 tabs
14 Week Visit	2 ml	2 x 25ml 1 x 240ml	2 ml clip	2.5 ml 1 tab	2 x 100ml 90 tabs
6 Month Visit	3 ml	4 x 25ml 1 x 240ml	3 ml clip	5 ml 2 tabs	5 x 100ml 180 tabs
9 Month Visit	4 ml	2 x 240ml	4 ml clip	5 ml 2 tabs	5 x 100ml 180 tabs
12 Month Visit	4 ml	2 x 240ml	4 ml clip	5 ml 2 tabs	5 x 100ml 180 tabs
Each subsequent 3m visit	4 ml	2 x 240ml	4 ml clip	5 ml 2 tabs	5 x 100ml 180 tabs

Annex 8 Cotrimoxazole Prophylaxis

INDICATIONS FOR COTRIMOXAZOLE USE AMONG CHILDREN

- All **HIV-exposed infants** from 6 weeks of age until HIV infection has been definitely ruled out **AND** the child is no longer breastfeeding.
- All children living with HIV should receive CTX prophylaxis for life.

CONTRAINDICATIONS FOR COTRIMOXAZOLE USE AMONG CHILDREN

CTX should not be started, or should be discontinued, if the child has:

- A severe adverse reaction to CTX or other sulfa-containing drugs (see below).
- Severe kidney (creatinine > 3x normal) and/or liver (LFTs > 5x normal) disease.

ALTERNATIVE PROPHYLAXIS WHEN COTRIMOXAZOLE IS CONTRAINDICATED

- Dapsone 2mg/kg once daily up to maximum of 100mg daily.

DISCONTINUATION OF COTRIMOXAZOLE PROPHYLAXIS

Exposed infants: Discontinue CTX when HIV infection has been definitely ruled out **AND** the child is no longer breastfeeding.

HIV-infected children: Discontinue if there is a severe adverse reaction to CTX, **or** if

- The child is overburdened by large number of tablets, AND
- s/he is over five years of age, AND
- there is evidence of immune recovery (CD4 > 350 for at least 6 months), AND
- there is NO history of PCP or toxoplasmosis.

INFORMATION FOR PARENTS

- Co-trimoxazole prevents serious infections in children exposed to and infected with HIV. It can help them feel better and live longer. It is not an antiretroviral drug, and does not treat or cure HIV infection.
- Exposed infants should be given CTX every day until they test HIV-negative AFTER breastfeeding cessation.
- HIV-infected children should take CTX every day for life.
- Co-trimoxazole tablet may be crushed and mixed with water or food.
- The dose will increase as the child grows.
- Children who develop adverse reactions to CTX should be taken to the nearest health facility as soon as possible.

COTRIMOXAZOLE TOXICITY GRADING

CTX Toxicity Grading and Recommendations		
Toxicity	Clinical Description	Recommendation
Grade 1	Mild red rash	Continue CTX with careful and repeated observation and follow-up. If available, provide symptomatic treatment such as antihistamines.
Grade 2	Diffuse red and/or bumpy rash, dry flaking skin	
Grade 3	Blistering of skin, mucosal ulceration	CTX should be permanently discontinued. Use dapsone as an alternative (dosing below). For children 12 years and older, desensitization can be considered (see adult guidelines).
Grade 4	Extensive nodular, target, or blistering skin lesions, moist peeling skin, mucosal ulceration, conjunctivitis, and/or Stevens-Johnson Syndrome	

COTRIMOXAZOLE PROPHYLAXIS DOSAGE

Once Daily Dosing for Cotrimoxazole (CTX, Bactrim, Cotrim, Cozole, TMP/SMX)				
Age	**Weight**	**Suspension 5ml (240mg/40mg)**	**Paediatric Tablet 100mg/20mg**	**Single strength Adult Tablet (400mg/80mg)**
Under 6 months	Under 5 kg	2.5ml	1	¼
6 months– 5 years	5 – 15 kg	5ml	2	½
6 Years- 14 years	15 – 30 kg	10ml	4	1
> 14 years	30 kg and over	-	-	2

Annex 9 WHO Clinical Staging for Infants and Children with HIV

Clinical Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage 2

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

Clinical Stage 3

- Moderate unexplained malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more)
- Unexplained persistent fever (above 37.5^{o} intermittent or constant, for longer than one month)
- Persistent oral candida (outside first 6- 8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis/periodontitis
- Lymph node TB
- Pulmonary tuberculosis
- Severe recurrent presumed bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (<8g/dl), neutropenia (<500/mm3) or chronic thrombocytopenia (<50 000/ mm3)
- HIV-associated cardiomyopathy or HIV-associated nephropathy

Clinical Stage 4

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe presumed bacterial infections (e.g., empyema, pyomyositis, bone or joint infection, meningitis; but excluding pneumonia)
- Chronic herpes simplex infection (orolabial/cutaneous of > 1 month's duration, or visceral at any site)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Oesophageal candidiasis (or candida of trachea, bronchi, or lungs)
- Central nervous system toxoplasmosis (outside the neonatal period)
- HIV encephalopathy
- Cytomegalovirus (CMV) retinitis or CMV infection affecting another organ, with onset at > 1 month of age
- Extrapulmonary cryptococcosis, including meningitis
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated non-tuberculous Mycobacteria infection
- Acquired HIV-associated rectal fistula
- Cerebral or B-cell non-Hodgkin lymphoma
- Progressive multifocal leukoencaephalopathy
- HIV associated rectovaginal fistula

Annex 10 HIV Staging Conditions in Infants and Children: Diagnostic Criteria and Management

Clinical Stage 1			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Asymptomatic	No HIV-related symptoms reported and no signs on examination.	Not required.	Cotrimoxazole prophylaxis
Persistent generalized lymphadenopathy (PGL)	Swollen or enlarged lymph nodes > 1 cm at two or more non-contiguous sites, without known cause.	Not required.	

Clinical Stage 2			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Unexplained persistent hepato-splenomegaly	Enlarged liver and spleen without obvious cause.	Not required.	
Papular pruritic eruptions (PPE)	Papular pruritic vesicular lesions. May be similar to scabies and insect bites, which are also common in uninfected children and should be excluded.	Not required.	Supportive skin care: - **Antihistamine** to treat pruritis (chlorpheniramine, promethazine, cetirizine, loratidine) - **Hydrocortisone 1%** cream applied once daily for no more than 5 to 7 days - Petroleum jelly, vegetable oil, lotion
Fungal nail infections	Fungal paronychia (painful, red and swollen nail bed) or onycholysis (painless separation of the nail from the nail bed). Proximal white subungual onychomycosis is uncommon without immunodeficiency.	Not required.	Topical antifungal treatment until resolution - **Miconazole** TDS - **Clotrimazole** TDS Griseofulvin if severe infection or no response to topical treatment
Angular cheilitis	Splits or cracks on lips at the angle of the mouth with depigmentation, usually responding to antifungal treatment but may recur.	Not required.	Topical antifungal therapy - **Clotrimazole** - **Nystatin** - **Ketoconazole**
Linear gingival erythema (LGE)	Erythematous band that follows the contour of the free gingival line; may be associated with spontaneous bleeding.	Not required.	Supportive Care & daily oral hygiene
Extensive wart virus infection	Characteristic warty skin lesions; small fleshy grainy bumps, often rough, flat on sole of feet (plantar warts); facial, more than 5% of body area or disfiguring.	Not required.	Antiretroviral therapy Dermatology referral - **Podophyllin** 10%-25% applied by practitioner then washed off 1-4 hours later, at 0.5 mL per treatment - Cauterisation
Extensive molluscum contagiosum infection	Characteristic skin lesions: small flesh-coloured, pearly or pink, dome-shaped or umbilicated growths, may be inflamed or red; facial, more than 5% of body area or disfiguring	Not required.	Antiretroviral therapy Gentle curettage
Recurrent oral ulcerations (two or more in six months)	Aphthous ulceration, typically with a halo of inflammation & yellow-grey pseudomembrane.	Not required.	Gentian violet Chlorhexidine solution mouth rinse
Unexplained parotid enlargement	Asymptomatic bilateral swelling that may spontaneously resolve and recur, in absence of other known cause, usually painless.	Not required.	Supportive care

Clinical Stage 2 (Continued)			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Herpes zoster	Painful rash with fluid-filled blisters, dermatomal distribution, can be haemorrhagic on erythematous background, and can become large and confluent. Does not cross the midline.	Not required.	Analgesia Moderate disease: oral **acyclovir** 80 mg/kg/day divided into 4-5 doses/day Severe disease: IV **acyclovir** 30 mg/kg/day divided every 8 hours
Recurrent upper respiratory tract infection (URTI)	Current event with at least one episode in past 6 months. Symptom complex; fever with unilateral face pain and nasal discharge (sinusitis) or painful swollen eardrum (otitis media), sore throat with productive cough (bronchitis), sore throat (pharyngitis) and barking croup-like cough (LTB). Persistent or recurrent ear discharge.	Not required.	Treat with standard antibiotics for suspected aetiology

Clinical Stage 3			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Unexplained moderate malnutrition	Weight loss: low weight-for-age, up to −2 standard deviations (SD), not explained by poor or inadequate feeding and/or other infections, and poor response to standard management	Confirmed by documented loss of body weight of –2SD, failure to gain weight on standard management and no other cause identified during investigation.	Nutritional support
Unexplained persistent diarrhoea	Unexplained persistent (14 days or more) diarrhoea (loose or watery stool, three or more times daily), not responding to standard treatment.	Confirmed by stools observed and documented as unformed. Culture and microscopy reveal no pathogens. Rule out Mycrosporidium	Nutritional support Rehydration - **Oral rehydration** - Intravenous if necessary Specific antibiotic treatment for suspected pathogen Antiretroviral therapy
Unexplained persistent fever (intermittent or constant, for longer than one month)	Reports of fever or night sweats for longer than one month, either intermittent or constant, with reported lack of response to antibiotics or antimalarials. No other obvious foci of disease reported or found on examination. Malaria must be excluded in malarious areas. Exclude TB.	Confirmed by documented fever of >37.5 ^{0}C with negative blood culture, negative malaria slide and normal or unchanged CXR, and no other obvious foci of disease.	Anti-pyretic - **Paracetamol** - **Ibuprofen** - **Mefenamic acid**
Oral candida (outside first 6-8 weeks of life)	Persistent or recurring creamy white to yellow soft small plaques which can be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender (erythematous form).	Confirmed by microscopy or culture.	Analgesia Antifungal therapy - **Nystatin oral solution** - **Miconazole gel** - **Clotrimazole** - **Fluconazole** if severe thrush or no response to topical therapy
Oral hairy leukoplakia	Fine small linear patches on lateral borders of tongue, generally bilaterally, which do not scrape off.	None.	ARV therapy
Lymph node TB	Non acute, painless "cold" enlargement of lymph nodes, usually matted, localized to one region. May have draining sinuses. Response to standard anti-TB treatment in one month.	Confirmed by histology or fine needle aspirate for Ziehl-Neelsen stain. Culture.	Anti-TB treatment Test and treat household contacts per national protocol
Pulmonary TB	Nonspecific symptoms: chronic cough, fever, night sweats, anorexia and weight loss. In the older child also productive cough and haemoptysis. Abnormal CXR. Response to standard anti-TB treatment in one month.	Confirmed by positive sputum smear or culture.	Anti-TB treatment Test and treat household contacts per national protocol

Clinical Stage 3 (Continued)			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Severe recurrent presumed bacterial pneumonia	Cough with fast breathing, chest indrawing, nasal flaring, wheezing, and grunting. Crackles or consolidation on auscultation. Responds to course of antibiotics. Current episode plus one or more in previous 6 months.	Confirmed by isolation of bacteria from appropriate clinical specimens (induced sputum, BAL, lung aspirate).	Supportive Care Antibiotic regimen appropriate for suspected pathogens
Acute necrotizing ulcerative gingivitis or stomatitis, or acute necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odour, and rapid loss of bone and/or soft tissue.	None.	Analgesia Appropriate antibiotics **Chlorhexidine** solution ARV therapy
Symptomatic LIP	No presumptive diagnosis.	Diagnosed by CXR: bilateral reticulonodular interstitial pulmonary infiltrates present for more than two months with no response to antibiotic treatment and no other pathogen found. Oxygen saturation persistently <90%. May present with cor pulmonale and may have increased exercise-induced fatigue. Characteristic histology.	Antibiotic treatment of superinfections **Prednisolone** - 1-2 mg/kg/day for 2-6 weeks - Titrate to lowest possible dose - Gradually taper over several weeks
Chronic HIV-associated lung disease (including bronchiectasis)	History of cough productive of copious amounts of purulent sputum (bronchiectasis only), with or without clubbing, halitosis, and crepitations and/or wheezes on auscultation.	Confirmed by CXR: may show honeycomb appearance (small cysts) and/or persistent areas of opacification and/or widespread lung destruction, with fibrosis and loss of volume.	Appropriate antibiotic therapy Supportive care ARV therapy
Unexplained anaemia (<8g/dl), or neutropenia (<1000/mm^3) or chronic thrombocytopenia (<50 000/ mm^3)	No presumptive diagnosis.	Diagnosed on laboratory testing. Not explained by other non-HIV conditions, or not responding to standard therapy with haematinics, antimalarials or anthelmintics as outlined in IMCI.	Nutritional support Vitamin supplementation Supportive care ARV therapy

Clinical Stage 4			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Unexplained severe wasting, stunting or severe malnutrition not adequately responding to standard therapy	Persistent weight loss not explained by poor or inadequate feeding or other infections, and not adequately responding to two weeks of standard therapy. Characterized by: visible severe wasting of muscles, with or without oedema of both feet, and/or weight-for-height of –3 SDs, as defined by WHO IMCI guidelines.	Confirmed by documented weight loss of >-3 SD +/- oedema.	Nutritional support ARV therapy
Recurrent severe presumed bacterial infection, e.g., empyema, pyomyositis, bone or joint infection, meningitis (but excluding pneumonia)	Fever accompanied by specific symptoms or signs that localize infection. Responds to antibiotics. Current episode plus one or more in previous 6 months.	Confirmed by culture of appropriate clinical specimen.	Analgesia Antipyretic Appropriate antibiotic regimen

Clinical Stage 4 (Continued)			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Pneumocystis pneumonia (PCP)	Dry cough, progressive difficulty in breathing, cyanosis, tachypnoea and fever; chest indrawing or stridor. (Severe or very severe pneumonia as in IMCI). Usually of rapid onset especially in infants under six months of age. Response to high-dose co-trimoxazole +/- prednisolone. (*For primary and secondary prophylaxis of PCP, see Annex 8)*	Confirmed by: CXR typical bilateral perihilar diffuse infiltrates; microscopy of induced sputum or BAL or NPA; or histology of lung tissue.	**Oxygen supplementation** **Cotrimoxazole** - 15-20 mg/kg/d (based on trimethoprim component) IV divided Q6-Q8 x 21 days **Corticosteroids** for severe disease - 1-2 mg/kg BD (max 40 mg) x 5 days, then 1-2 mg/kg OD (max 40 mg) x 5 days, then 0.5-1 mg/kg OD (max 20 mg) to completion of treatment **Clindamycin** - 25-40 mg/kg/day IV/IM divided every 6-8 hours, max 4.8 g/d - 10-30 mg/kg/d PO div q6-8 h, max 1.8 g/d
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration or visceral at any site)	Severe and progressive painful orolabial, genital, or anorectal lesions caused by HSV infection present for more than one month.	Confirmed by culture and/or histology.	Analgesia; antipyretic Treatment - Mild: oral **acyclovir** 40-80 mg/kg/day divided TDS for 7 to 10 days (maximum 1200 mg/kg/day) - Severe: IV **acyclovir** 15-30 mg/kg/day divided TDS, given over one hour, for 7 to 14 days
Oesophageal candida (or candida of trachea, bronchi or lungs)	Chest pain and dysphagia (difficulty in swallowing), odynophagia (pain on swallowing food and fluids), or retrosternal pain worse on swallowing (food and fluids); responds to specific treatment. In young children, suspect particularly if oral candida observed and food refusal occurs and/or difficulties/crying when feeding.	Confirmed by macroscopic appearance at endoscopy, microscopy of specimen from tissue, macroscopic appearance at bronchoscopy, or histology.	Analgesia Antifungal - **Fluconazole** Loading dose: 10 mg/kg IV/PO Maintenance (24 hours after loading dose) 3-6 mg/kg/day IV/PO OD, max 12 mg/kg/day x 4 days - **Ketoconazole** 3 to 6 mg/kg/d x 5 days (pre-ART only)
Extrapulmonary/ disseminated TB	Systemic illness usually with prolonged fever, night sweats, weight loss. Clinical features of organs involved, e.g., sterile pyuria, pericarditis, ascites, pleural effusion, meningitis, arthritis, orchitis. Responds to standard anti-TB therapy.	Confirmed by positive microscopy showing AFB or culture of Mycobacterium TB from blood or other relevant specimen (except sputum or BAL). Biopsy and histology.	Anti-TB as per national protocol
Kaposi sarcoma	Typical appearance in skin or oropharynx of persistent, initially flat, patches with a pink or blood-bruise colour, skin lesions that usually develop into nodules.	Not required but may be confirmed by : - typical red-purple lesions seen on bronchoscopy or endoscopy; - dense masses in lymph nodes, viscera, or lungs by palpation or radiology; - histology.	Antiretroviral therapy containing lamivudine and consider **lopinavir/ritonavir** if possible Refer for chemotherapy
CMV retinitis or CMV infection affecting another organ, with onset at age over 1 month.	Retinitis only. CMV retinitis may be diagnosed by experienced clinicians: progressive floaters in field of vision, light flashes and scotoma; typical eye lesions on serial fundoscopic examination; discrete patches of retinal whitening with distinct borders, spreading centrifugally, often following blood vessels, associated with retinal vasculitis, haemorrhage, and necrosis.	Definitive diagnosis required for other sites. Histology. CSF polymerase chain reaction (PCR).	Treatment - **Ganciclovir**: 5 mg/kg BID IV x 14 days Secondary Prophylaxis - <12 years old: **Ganciclovir** 5 mg/kg/dose OD IV or 6 mg/kg/dose IV OD x 5 days per week - >12 years old: **Ganciclovir** 1000 mg PO TDS with food

Clinical Stage 4 (Continued)			
Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
CNS toxo-plasmosis with onset at age over 1 month	Fever, headache, focal neurological signs, convulsions. Usually responds within 10 days to specific therapy.	Not required but confirmed by computed tomography (CT) scan showing single/multiple lesions with mass effect, enhancing with contrast.	**Dexamethasone** or corticosteroids for cerebral edema or mass effect. **Children <12 years old**: - **Pyrimethamine** 1-2 mg/kg PO BD x 2 days then 1 mg/kg/day PO x 2 months then 1 mg/kg/day PO 3 days/ week (max 50 mg) then 0.5 mg/kg PO BD x 4 weeks **AND** - **Sulfadiazine** 100 mg/kg oral loading dose then 50 mg/kg PO BD **AND** - **Folinic acid** 5-10 mg PO/IM 3 times/week **Children >12 years old:** - **Pyrimethamine** 200 mg PO loading dose then 50-100 mg PO OD **AND** - **Folinic acid** 10 mg PO OD **AND** - **Sulfadiazine** 1-1.5 g PO q 6 hours **OR/PLUS** - **Clindamycin** 600 mg PO/IV q 6 hours **Primary Prophylaxis:** Same as PCP **Secondary Prophylaxis (**for life) **<12 years old:** - **Pyrimethamine**: 1 mg/kg PO OD (max 25 mg) AND - **Sulfadiazine** 40 mg/kg/day PO div. 3 times per day AND - **Folinic acid** 5 mg PO every 3 days **>12 years old:** - **Pyrimethamine** 25 mg PO OD **AND** - **Sulfadiazine** 1000 mg PO TDS **AND** - **Folinic acid** 15 mg PO OD
Extra-pulmonary crypto-coccosis, including meningitis	Meningitis: usually sub-acute, fever with increasing severe headache, meningism, confusion, behavioural changes that responds to cryptococcal therapy.	Confirmed by CSF microscopy (India ink or Gram stain), serum or CSF cryptococcal antigen (CRAG) or culture.	**Treatment** - **Amphotericin B** 0.7 mg/kg/day IV diluted in Dextr 5% (Anphotericin precipitates in Salt solutions) x 14 days (start with test dose of 0.1 mg/kg IV over 20 minutes, then remainder of 1st dose), max. 1.5 mg/kg/day. Give normal saline 10 ml/kg before and after giving Ampho B infusion to reduce risk of renal toxicity. ADDITIONALLY: - AFTER 14 DAYS **Fluconazole** 12 mg/kg/day for 8-10 weeks, then suppressive therapy (max 600 mg/day for children, 400 mg/day for adolescents) **Alternative regimen** - **Fluconazole** 12 mg/kg PO/IV x 1, then 6 mg/kg/day until 10-12 wks after negative cultures, then suppressive therapy **Secondary Prophylaxis (suppresssive regimen)** - **Fluconazole** 6 mg/kg/day for life
HIV encephal-opathy	At least one of the following, progressing over at least 2 months in the absence of another illness: - failure to attain, or loss of, developmental milestones or intellectual ability; **or** - progressive impaired brain growth demonstrated by stagnation of head circumference; **or** - acquired symmetric motor deficit accompanied by two or more of the following: paresis, pathological reflexes, ataxia, abnormal gait.	Confirmed by brain CT scan or MRI demonstrating atrophy and basal ganglia calcification and excluding other causes.	ARV therapy

Clinical Stage 4 (Continued)			
Clinical event	**Clinical Diagnosis**	**Definitive Diagnosis**	**Treatment and Prophylaxis**
Disseminated mycosis (coccidiomycosis, histoplasmosis, penicilliosis)	No presumptive diagnosis.	Diagnosed by: - Histology: usually granuloma formation. - Isolation: antigen detection from affected tissue; culture or microscopy from clinical specimen or blood culture.	**Treatment:** **Amphotericin** followed by **fluconazole** **Secondary prophylaxis** for life
Disseminated mycobacteriosis, other than TB	No presumptive diagnosis.	Nonspecific clinical symptoms including progressive weight loss, fever, anaemia, night sweats, fatigue or diarrhoea; plus culture of atypical Mycobacteria species from stool, blood, body fluid or other body tissue, excluding lung.	For MAC: - **Clarithromycin** 7.5 mg/kg (max 500 mg) PO BD PLUS - **Ethambutol** 15-25 mg/kg day PO OD (max 1 g/day) - If unresponsive may add r**ifampicin** **Primary Prophylaxis** - **Clarithromycin** 7.5 mg/kg/dose PO BID (max 1 g/day) OR **Secondary Prophylaxis** may be stopped in >12 years old after 12 months of ART and CD4 count >100 cells/uL for 6 months Same as primary prophylaxis but must add **ethambutol** 15 mg/kg/dose PO OD (max 900 mg/dose)
Chronic cryptosporidiosis	No presumptive diagnosis.	Confirmed in children with chronic diarrhoea lasting longer than one month by microscopic examination.	Antiretroviral therapy **Cotrimoxazole** 6 to 10 mg/kg/day TMP PO div. BD x 2 to 4 weeks AND Metronidazole 30 mg/kg/day div. TDS x 2 to 4 weeks Nutritional supplementation Supportive care
Chronic *Isospora*	No presumptive diagnosis.	Confirmed in children with chronic diarrhoea by microscopic examination.	**Cotrimoxazole** 6 to 10 mg/kg/day TMP PO div. BD x 2 to 4 weeks, max 1 DS tablet PO BD Antiretroviral therapy
Cerebral or B-cell non-Hodgkin lymphoma	No presumptive diagnosis.	Diagnosed by CNS imaging: at least one lesion with mass effect on brain scan; histology of relevant specimen.	Chemotherapy
Progressive multifocal leukoencephalopathy (PML)	No presumptive diagnosis.	Diagnosed by MRI or CT scan, and biopsy. Viral PCR for Jacob-Creutzfeldt virus.	Antiretroviral therapy
HIV-associated rectovaginal fistula	GU examination reveals connection between vaginal and rectal canals	Clinical confirmation	Refer for surgical intervention.

Annex 11 Pre ART Adherence Counselling Topics

HIV/AIDS

- ❑ Basic education about HIV
- ❑ Education that HIV is now a chronic illness and is no longer fatal if treated and monitored properly

ARVs

- ❑ Basic education about ARVs and their function
- ❑ ARVs, used properly, prolong survival and improve quality of life
- ❑ ARVs are not a cure for HIV, they suppress the amount of HIV to a harmless level if taken properly
- ❑ ARVs once started are taken for life
- ❑ ARVs have known side effects that require regular follow-up with a physician

Adherence

- ❑ Excellent adherence to a regimen guarantees greater success of therapy
- ❑ Patient and caregiver willingness and commitment to treatment plan
- ❑ Disclosure to family and family dynamics
- ❑ The caretaker's role in the ARV therapy and adherence
- ❑ Explanation and demonstration of correct administration of medicines to the child, especially use of syringes, measuring spoons or caps
- ❑ Explanation and demonstration of practical medication management tools (pill boxes, timers (e.g. cell phone reminders), medication diaries)
- ❑ Importance of financial and social support of the treatment
- ❑ Accessibility to health care site for refills

Positive Living

- ❑ Mechanisms to cope with HIV/AIDS and lifelong treatment
- ❑ Importance of positive living
- ❑ Importance of educational and recreational needs of the child
- ❑ Education and motivation about responsible sexual behaviour, e.g. delay of sexual encounter or abstinence, use of safer sexual practices in adolescents and sexually active youth
- ❑ Reproductive health counselling and family planning options
- ❑ Safer infant feeding options
- ❑ The child should not be limited in participating in activities unless medically contraindicated by the health care worker

Annex 12 Common ARV Formulations Available in Swaziland

The following ARV formulations are available in Swaziland for common paediatric first- and second-line regimens. Use fixed dose combination (FDC) tablets whenever possible. Single ARV medications and additional formulations may be available. Check with Central Medical Stores for availability.

ARVs	Formulation	Common Names
AZT + 3TC	Paediatric (60/30)	AZT Dual
	Adult (300/150)	Zidolam, Avacomb, Combivir
AZT+3TC+NVP	Paediatric (60/30/50)	AZT Triple
	Adult (300/150/200)	Zidolam – N, Avacomb – N
D4T+3TC	Paediatric (12/60)	Lamivir Junior
	Adult (30/150)	Coviro
D4T+3TC+NVP	Paediatric (12/60/100)	Triomune Junior (FDC 12)
	Adult (30/150/200)	Triomune 30, Triviro, Triomune-LNS
ABC+3TC	Paediatric (60/30)	
	Adult (600/300)	
TDF+3TC	Adult (300/300)	
TDF+3TC+EFV	Adult (300/300/600)	
EFV	Paediatric (50mg, 100mg, 200mg) Adult (600mg)	
LPV/r	Syrup (80/20) Tablet (100/25, 200/50)	Kaletra Alluvia
ddI	Syrup (10mg/ml) Chewable Tab (25mg) Enteric Coated Tab (125mg, 200mg)	
Ritonavir	Capsules (100mg)	Use for boosting LPV/r to 1:1 ratio during TB treatment

Annex 13 Weight-Based ARV Dosing For Common Paediatric Regimens

ART Regimen	3-3.9kg	4-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg	25-39.9 kg	40 kg and over
AZT/3TC/NVP (60/30/50) Triple Paed FDC	1 BD	1 BD	1½ BD	2 BD	2½ BD	3 BD	Adult FDC 1 bd	Adult FDC 1 bd
d4T/3TC/NVP (12/60/100) Triple Junior FDC	½ BD	½ BD	1 AM, ½PM	1 BD	1½ AM, 1 PM	1½ BD	Adult FDC 1 bd	Adult FDC 1 bd
AZT/3TC (60/30) Dual Paed FDC	1 BD	1 BD	1½ BD	2 BD	2½ BD	3 BD	Adult Dual 1 BD	Adult Dual 1 BD
d4T/3TC (12/60) Dual Junior FDC	½ BD	½ BD	1 AM, ½PM	1 BD	1½ AM, 1 PM	1½ BD	Adult Dual 1 BD	Adult Dual 1 BD
EFV	Not recommended			200mg nocte	300mg nocte	300mg nocte	400mg nocte	600mg nocte
LPV/r	1 ml 80/20mg syr	1½ ml 80/20mg syr	1½ ml 80/20mg syr	2ml syrup **or** 2AM, 1 PM 100/25 tab	2 BD 100/25 tab **or** 1 BD 200/50 tab	3 AM, 2PM 100/25 tab **or** 2 AM, 1PM 200/50 tab	3 BD 100/25 tab or 2 AM, 1PM 200/50 tab	4 BD 100/25 tab or 2 BD 200/50 tab
ABC/3TC (60/30) Mainly used in second-line	1 BD	1 BD	1½ BD	2 BD	2½ BD	3 BD	Adult Dual 1 BD	Adult Dual 1 BD
ddI **Alternate second-line**	Not recommended		3 AM, 2 PM 25mg chew tab	1 OD 125mg EC cap	1 OD 200mg EC cap	2 OD 125mg EC cap	2 OD 125mg EC cap	2 OD 200mg EC cap

Annex 14 General Grading of ARV Side Effects and Toxicities

Mild side effects such as headache, fatigue, gastrointestinal upsets and diarrhoea occur early and fairly frequently, often wear off, and should be treated symptomatically. Serious toxicities occur rarely, but are important to recognize because they may be life threatening. Grading of side effects and toxicities guides management and helps determine whether or not ARV substitution is necessary.

Grade	Description	Action
Grade 1 **Mild**	Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required	• Child remains on therapy. • Repeat the test. • Reassess clinically within 2 weeks
Grade 2 **Moderate**	Mild to moderate limitation in activity-some assistance may be needed; no or minimal medical intervention/therapy required.	• Child remains on therapy. • Repeat the test. • Reassess clinically within 2 weeks
Grade 3 **Severe**	Marked limitation in activity; assistance usually required; medical intervention/therapy required; hospitalization possible.	• Test/exam should be repeated within 1 week. • If still Grade 3, stop all antiretroviral drugs and seek expert medical advice.
Grade 4 **Life-threatening**	Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required; hospitalization or hospice care probable.	• 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.

Annex 15 Severity Grading of common toxicities seen with ARVs for children

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access. Recommendations for a public health approach. 2010.

PARAMETER	MILD (grade 1)	MODERATE (grade 2)	SEVERE (grade 3)	SEVERE AND POTENTIALLY LIFE-THREATENING (grade 4)
GENERAL GUIDANCE ON ESTIMATING SEVERITY GRADE				
Characterization of symptoms and general guidance on management	Symptoms causing no or minimal interference with usual social and functional activities: [a] no therapy needed, monitor	Symptoms causing greater than minimal interference with usual social and functional activities: may require minimal intervention and monitoring	Symptoms causing inability to perform usual social and functional activities: requires medical care and possible hospitalization	Symptoms causing inability to perform basic self-care functions: [c] requires medical or operative intervention to prevent permanent impairment, persistent disability or death
HAEMATOLOGY (Standard international units are listed in italics)				
Absolute neutrophil count	750 – <1000/mm^3 *0.75 x 10^9 – <1 x 10^9/L*	500 – 749/mm^3 *½ x 10^9 – 0.749 x 10^9/L*	250 – 500/mm^3 *0.25 x 10^9 –½ x 10^9/L*	<250/mm^3 *<0.250 x 10^9/L*
Haemoglobin (child >60 days of age)	8.5 – 10.0 g/dl *1.32 – 1.55 mmol/L*	7.5–<8.5 g/dl *1.16 – <1.32 mmol/L*	6.5 – <7.5 g/dl *1.01 – <1.16 mmol/L*	<6.5 g/dl *<1.01 mmol/L* Or severe clinical symptoms attributable to anaemia (e.g. cardiac failure), refractory to supportive therapy
Platelets	100 000–<125 000/mm^3 *100 x 10^9 – 125 x 10^9/L*	50 000–<100 000/mm^3 *50 x 10^9 – <100 x 10^9/L*	25 000–<50 000/mm^3 *25 x 10^9 – <50 x 10^9/L*	<25 000/mm^3 *<25 x 10^9/L* Or bleeding
GASTROINTESTINAL				
Laboratory				
ALT (SGPT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	>10.0 x ULN
AST (SGOT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	>10.0 x ULN
Bilirubin (>2 weeks of age)	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	>5.0 x ULN
Lipase	1.1 – 1.5 x ULN	1.6 – 3.0 x ULN	3.1 – 5.0 x ULN	>5.0 x ULN
Pancreatic amylase	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	2.1 – 5.0 x ULN	>5.0 x ULN
Clinical				

[a] Values are provided for children in general except where age groups are specificied.
[b] Usual social and functional activities in young children include those that are appropriate for their age and culture (e.g. social interactions, play activities, learning tasks).
[c] Activities that are appropriate for age and culture (e.g. feeding self with culturally appropriate eating implement, walking or using hands).

PARAMETER	MILD (grade 1)	MODERATE (grade 2)	SEVERE (grade 3)	SEVERE AND POTENTIALLY LIFE-THREATENING (grade 4)
Diarrhoea ≥1 year of age <1 year of age	Transient or intermittent episodes of unformed stools OR increase of ≤3 stools over baseline per day Liquid stools (more unformed than usual) but usual number of stools	Persistent episodes of unformed to watery stools OR increase of 4 – 6 stools over baseline per day Liquid stools with increased number of stools OR mild dehydration	Grossly bloody diarrhoea OR increase of ≥7 stools per day OR intravenous fluid replacement indicated Liquid stools with moderate dehydration	Life-threatening consequences (e.g. hypotensive shock) Liquid stools resulting in severe dehydration with aggressive rehydration indicated OR hypotensive shock
Nausea	Transient (<24 hours) or intermittent nausea with no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24 – 48 hours	Persistent nausea resulting in minimal oral intake for >48 hours OR aggressive rehydration indicated (e.g. intravenous fluids)	Persistent nausea with no or minimal oral intake resulting in dehydration with aggressive rehydration indicated
Pancreatitis	Not applicable	Symptomatic AND hospitalization not indicated (other than emergency treatment)	Symptomatic AND hospitalization not indicated (other than emergency treatment)	Life-threatening consequences (e.g. circulatory failure, haemorrhage, sepsis)
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting resulting in orthostatic hypotension OR aggressive rehydration indicated (e.g. intravenous fluids)	Life-threatening consequences (e.g. hypotensive shock)
ALLERGIC/DERMATOLOGICAL				
Acute systemic allergic reaction	Localized urticaria (weals) lasting a few hours	Localized urticaria with medical intervention indicated OR mild angioedema	Generalized urticaria OR angioedema with medical intervention indicated OR symptomatic mild bronchospasm	Acute anaphylaxis OR life-threatening bronchospasm or laryngeal oedema

PARAMETER	MILD (grade 1)	MODERATE (grade 2)	SEVERE (grade 3)	SEVERE AND POTENTIALLY LIFE-THREATENING (grade 4)
Cutaneous reaction – rash	Localized macular rash	Diffuse macular, maculopapular, or morbilliform rash OR target lesions	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR superficial ulcerations of mucous membrane limited to one site	Extensive or generalized bullous lesions OR Stevens – Johnson syndrome OR ulceration of mucous membrane involving two or more distinct mucosal sites OR toxic epidermal necrolysis (TEN)
NEUROLOGICAL				
Alteration in personality, behaviour or mood[b]	Alteration causing no or minimal interference with usual social and functional activitiesb	Alteration causing greater than minimal interference with usual social and functional activities[b]	Alteration causing inability to perform usual social and functional activities[b] AND intervention indicated	Behaviour potentially harmful to self or others OR life-threatening consequences
Altered mental status	Changes causing no or minimal interference with usual social and functional activities[b]	Mild lethargy or somnolence causing greater than minimal interference with usual social and functional activities[b]	Onset of confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social and functional activities[b]	Onset of delirium, obtundation or coma
Neuromuscular weakness (including myopathy and neuropathy)	Asymptomatic with decreased strength on examination OR minimal muscle weakness causing no or minimal interference with usual social and functional activities[b]	Muscle weakness causing greater than minimal interference with usual social and functional activities[b]	Muscle weakness causing inability to perform usual social and functional activities[b]	Disabling muscle weakness causing inability to perform basic self-care functions OR respiratory muscle weakness impairing ventilation

[b] Usual social and functional activities in young children include those that are appropriate for their age and culture (e.g. social interactions, play activities, learning tasks).

PARAMETER	MILD (grade 1)	MODERATE (grade 2)	SEVERE (grade 3)	SEVERE AND POTENTIALLY LIFE-THREATENING (grade 4)
Neurosensory alteration (including painful neuropathy)	Asymptomatic with sensory alteration on examination OR minimal paraesthesia causing no or minimal interference with usual social and functional activities	Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities	Sensory alteration or paraesthesia causing inability to perform usual social and functional activities	Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions[c]
OTHER LABORATORY PARAMETERS (Standard international units are listed in italics)				
Cholesterol (fasting, paediatric <18 years old)	170–<200 mg/dl *4.40 – 5.15 mmol/L*	200 – 300 mg/dl *5.16 – 7.77 mmol/L*	>300 mg/dl *>7.77 mmol/L*	Not applicable
Glucose, serum, high: non-fasting	116 – <161 mg/dl *6.44 – <8.89 mmol/L*	161 – <251 mg/dl *8.89 – <13.89 mmol/L*	251 – 500 mg/dl *13.89 – 27.75 mmol/L*	>500 mg/dl *>27.75 mmol/L*
Glucose, serum, high: fasting	110 – <126 mg/dl *6.11 – <6.95 mmol/L*	126 – <251 mg/dl *6.95 – <13.89 mmol/L*	251 – 500 mg/dl *13.89 – 27.75 mmol/L*	>500 mg/dl *>27.75 mmol/L*
Lactate	<2.0 x ULN without acidosis	≥2.0 x ULN without acidosis	Increased lactate with pH <7.3 without life-threatening consequences or related condition present	Increased lactate with pH <7.3 with life-threatening consequences (e.g. neurological findings, coma) or related condition present
Triglycerides (fasting)	Not applicable	500 – <751 mg/dl *5.65 – <8.49 mmol/L*	751 – 1 200 mg/dl *8.49 – 13.56 mmol/L*	>1 200 mg/dl *>13.56 mmol/L*

Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004.

Interactions, play activities, learning tasks).

[c] Activities that are appropriate for age and culture (e.g. feeding self with culturally appropriate eating implement, walking or using hands).

Annex 16 Management of Serious Acute and Chronic ARV Toxicities

Source: WHO. Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access. Recommendations for a public health approach. 2010.

Alternative explanations for toxicity must be excluded before concluding that symptoms are secondary to the ARV drug. This table describes management of the ART regimen but does not indicate detailed clinical toxicity management.

Possible clinical manifestations (most common ARV drug or drugs associated with the toxicity)	Possible laboratory abnormalities [a]	Implications for ARV drug treatment
Acute serious adverse reactions		
Acute, symptomatic hepatitis (NNRTI class, particularly NVP, more rarely EFV; NRTIs or PI class		
• Jaundice • Liver enlargement • Gastrointestinal symptoms • Fatigue, anorexia • May have hypersensitivity component (rash, fever, systemic symptoms), usually occurs within 6–8 weeks • May have accompanying lactic acidosis (*see below*) if secondary to NRTI drug	• Elevated transaminases • Elevated bilirubin	• Discontinue all ARVs until symptoms resolve • If possible, monitor transaminases, bilirubin • If receiving NVP, it should NOT be readministered to the patient in future • Once symptoms resolve, either: – restart ART with substitution to alternative ARV (if on NVP regimen, this is required); or – restart same ART regimen with close observation; if symptoms recur, substitute an alternative ARV [b]
Acute pancreatitis (NRTI class, particularly d4T, ddI; more rarely 3TC)		
• Severe nausea and vomiting • Severe abdominal pain • May have accompanying lactic acidosis (*see below*)	• Elevated pancreatic amylase • Elevated lipase	• Discontinue all ARVs until symptoms resolve • If possible, monitor serum pancreatic amylase, lipase • Once symptoms resolve, restart ART with substitution of an alternative NRTI, preferably one without pancreatic toxicity [b]

Possible clinical manifestations (most common ARV drug or drugs associated with the toxicity)	Possible laboratory abnormalities [a]	Implications for ARV drug treatment
Hypersensitivity reaction (ABC or NVP)		
• *ABC:* Combination of acute onset of both respiratory and gastrointestinal symptoms after starting ABC, including fever, fatigue, myalgia, nausea, vomiting, diarrhoea, abdominal pain, pharyngitis, cough, dyspnoea; rash (usually mild) may or may not occur; progressive worsening of symptoms soon after receiving ABC dose, usually occurs within 6–8 weeks • *NVP:* Systemic symptoms of fever, myalgia, arthralgia, hepatitis, with or without rash usually occurs within 6–8 weeks	• Elevated transaminases • Elevated eosinophil count	• Immediately discontinue all ARVs until symptoms resolve • NVP or ABC should NOT be readministered to the patient in future • Once symptoms resolve, restart ART with substitution of an alternative ARV for ABC or NVP[b]
Lactic acidosis (NRTI class, particularly d4T)		
• Generalized fatigue and weakness • Gastrointestinal features (nausea, vomiting, diarrhoea, abdominal pain, hepatomegaly, anorexia, poor weight gain and/or sudden unexplained weight loss) • May have hepatitis or pancreatitis (see above) • Respiratory features (tachypnoea and dyspnoea) • Neurological symptoms (including motor weakness) Can occure at any time on ART	• Increased anion gap • Lactic acidosis • Elevated aminotransferase • Elevated creatine phospholkinase (CPK) • Elevated lactate dehydrogenase (LDH)	• Discontinue all ARVs until *symptoms* resolve • Symptoms associated with lactic acidosis may continue or worsen despite discontinuation of ART • Once symptoms resolve, restart ART with substitution of an alternative NRTI with lower mitochondrial toxicity risk (e.g. ABC or AZT[b]

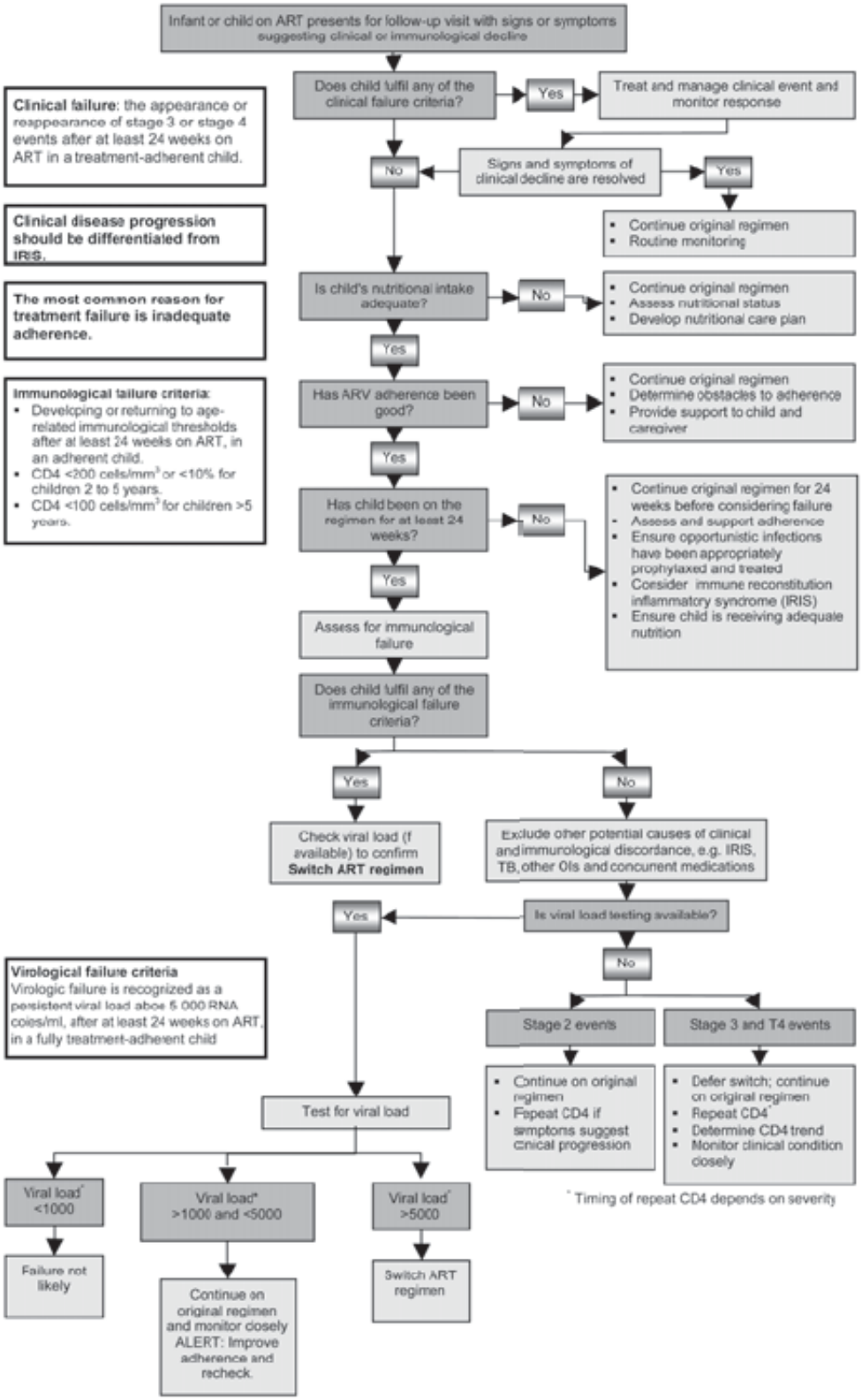
Possible clinical manifestations (most common ARV drug or drugs associated with the toxicity)	Possible laboratory abnormalities [a]	Implications for ARV drug treatment
Severe rash/Stevens – Johnson syndrome (NNRTI class, particularly NVP, less common EFV)		
• Rash usually occurs during first 6–8 weeks of treatment • *Mild-to-moderate rash:* erythematous, maculopapular, confluent, most often on the body and arms, with no systemic symptoms • *Severe rash:* extensive rash with moist desquamation, angioedema, or serum sickness-like reaction; or rash with constitutional findings such as fever, oral lesions, blistering, facial oedema, conjunctivitis • Life-threatening Stevens–Johnson syndrome or toxic epidermal necrolysis (TEN)	• Elevated transaminases	• If mild or moderate rash, ART can continue without interruption staying at induction dose until rash settles but with close observation, and only increase to maintenance dose once tolerated • For severe or life-threatening rash, discontinue all ARVs until symptoms resolve • NVP should NOT be readministered to the patient in the future • Once symptoms resolve, restart ART with substitution of an alternative ARV for NVP (note: most experts would not change to another NNRTI drug if patient had severe or life-threatening Stevens – Johnson syndrome with NVP) [b]
Severe life-threatening anaemia (AZT)		
• Severe pallor, tachycardia • Significant fatigue • Congestive heart failure	• Low haemoglobin	• refractory to symptomatic treatment (e.g. transfusion), discontinue AZT only and substitute an alternative NRTI [b]
Severe neutropenia (AZT)		
• Sepsis/infection	• Low neutrophil count	• If refractory to symptomatic treatment (e.g. transfusion), discontinue AZT only and substitute an alternative NRTI [b]

Possible clinical manifestations (most common ARV drug or drugs associated with the toxicity)	Possible laboratory abnormalities [a]	Implications for ARV drug treatment
Chronic late serious adverse reactions		
Lipodystrophy/metabolic syndrome (d4T; PIs)		
• Fat accumulation and/or fat loss in distinct regions of the body: – increased fat around the abdomen, buffalo hump, breast hypertrophy – fat loss from limbs, buttocks and face occurs to a variable extent • Insulin resistance, including diabetes mellitus • Potential risk for later coronary artery disease	• Hyper-triglyceridaemia • Hyper-cholesterolaemia; • Low high-density lipoprotein (HDL) levels • Hyperglycaemia	• Substitution of ABC or AZT for d4T may prevent progression of lipoatrophy • Substitution of an NNRTI for a PI may decrease serum lipid abnormalities
Severe peripheral neuropathy (d4T, ddI; more rarely 3TC)		
• Pain, tingling, numbness of hands or feet; inability to walk • Distal sensory loss • Mild muscle weakness and areflexia may occur	• None	• Stop suspected NRTI only and substitute a different NRTI that is not associated with neurotoxicity b • Symptoms may take several weeks to resolve

[a] All laboratory abnormalities may not be observed.

[b] See Table 7 (Section 9) for recommended ARV drug substitutions.

Annex 17 Algorithm for Assessing and Managing Treatment Failure



WHO. Antiretroviral Therapy for HIV Infection in Infants and Children: Towards Universal Access. 2010 Revision.

Annex 18 Pediatric Dosing of Essential Medicines for Common Illnesses

Drug	Dose	Formulation	
Acyclovir	VZV: 80mg/kg/day po div q6h x 5-7 days	Tab	200mg, 400mg, 800mg
Albendazole	1-2 years: 200mg po x 1 >2 years: 400mg po x 1	Tab	100mg, 200mg
Amoxicillin	80-100mg/kg/day po div BD-TDS (max 2-3g/day)	Tab Susp	250 mg 125mg/5 mL
Augmentin	30-90 mg/kg/day po div BD-TDS	Tab Suspension	375mg, 625mg 125-31.25mg/5ml
Cefaclor	20-40mg/kg/day div q6h	Tab Syr	375mg 187mg/5ml
Ceftriaxone	50–75 mg/kg/24 hr QD IM/IV (max 2g/24 hr); Meningitis: 100 mg/kg/24 hr IM/IV÷BD; (max 4g/24 hr)	Inj	1 G
Chloramphenacol	IM: 50-100mg/kg/day div q6h (max 4g/day); PO: 50-75mg/kg/day div q6	Capsule Suspension	250mg 125mg/5ml
Chlorpheniramine (Allergex)	2-6yrs: 1mg/dose PO q4-6hr (max 6mg/day) 6-11yrs: 2mg/dose PO q4-6hr (max 12mg/day) >12yrs: 4mg/dose q4-6hr (max 24mg/day)	Tab	4mg
Ciprofloxacin	20-30mg/kg/day BD (max 1.5g/day)	Tab	250mg, 500mg
Cloxacillin	25-100mg/kg/day PO q6h (max 4g/day)	Capsules Suspension	250mg 125mg/5ml
Cotrimoxazole (based on TMP)	Treatment: 8-10mg/kg/day BD PCP Tx: 20mg/kg/day PO/IV TDS	Tab (SS) Suspension	80mg/400mg TMP/S 40mg/200mg / 5mL
Diclofenac	2-3mg/kg/day div BD-QDS (max 100mg/day)	Injection	75mg/3ml
Erythromycin	30-50mg/kg/day po div TDS-QDS (max 2g/day)	Tab Suspension	250mg 125mg/5ml
Ferrous Sulfate	3-6mg elem Fe/kg/day PO	Tab	200mg (60mg elem Fe)
Fluconazole	6-12mg/kg load dose then 3-6mg/kg OD (max 400/d)	Tab	200mg
Ketoconazole	>2yrs: 3.3-6.6mg/kg/day po OD (max 800mg/day)	Tab	200mg
Griseofulvin	>2yrs: 20-25mg/kg/day po div OD (max 1g/day)	Tab	125mg, 500mg
Magnesium Hydroxide	<2yrs: 0.5ml/kg/day po div QD-QDS >2yrs: 5-60ml/day po div QD-QDS		
Mefanamic Acid	20mg/kg/day div. TDS (max 500mg tid)		50mg/5ml
Metronidazole	15-50mg/kg/day PO div TDS (max 2.25g/day)	Tab Suspension	200mg 125mg/5ml
Panadol	15mg/kg/dose PO q4hours (max 4grams/day)	Syrup Tab	120mg/5ml 500 mg
Promethazine	>2yrs: 0.1-1mg/kg/dose PO q4hrs (max 25mg pot id)	Susp Tab	5mg/5ml 25mg
Salbutamol	<6yrs: 0.3mg/kg/day po div TDS 6-11yrs: 6mg/24hrs po div TDS >12yrs: 2-4mg PO TDS-QDS (max 32mg/day)	Syrup Tab	2mg/5ml 4mg

Annex 19 WHO Weight for Height Tables for Infants and Children

Weight for Height Table Boys and Girls (49cm-130cm)*

WEIGHT-FOR-LENGTH								WEIGHT-FOR-LENGTH						
			Malnutrition								Malnutrition			
			Moderate Wasting 70 to 79%		Severe Wasting <%70						Moderate Wasting 70 to 79%		Severe Wasting <%70	
Height	100%	85%	80%	75%	70%	60%		Height	100%	85%	80%	75%	70%	60%
(cm)	In Kg	in Kg	in Kg	in Kg	in Kg	in Kg		(cm)	in Kg	in Kg	in Kg	in Kg	in Kg	in Kg
49.0	3.2	2.7	2.6	2.4	2.3	1.9		**67.0**	7.6	6.5	6.1	5.7	5.3	4.6
49.5	3.3	2.8	2.6	2.5	2.3	2.0		**67.5**	7.8	6.6	6.2	5.8	5.4	4.7
50.0	3.4	2.9	2.7	2.5	2.4	2.0		**68.0**	7.9	6.7	6.3	5.9	5.5	4.7
50.5	3.4	2.9	2.7	2.6	2.4	2.0		**68.5**	8.0	6.8	6.4	6.0	5.6	4.8
51.0	3.5	3.0	2.8	2.6	2.5	2.1		**69.0**	8.2	7.0	6.6	6.1	5.7	4.9
51.5	3.6	3.1	2.9	2.7	2.5	2.2		**69.5**	8.3	7.1	6.7	6.2	5.8	5.0
52.0	3.7	3.1	3.0	2.8	2.6	2.2		**70.0**	8.5	7.2	6.8	6.3	5.9	5.1
52.5	3.8	3.2	3.0	2.8	2.6	2.3		**70.5**	8.6	7.3	6.9	6.4	6.0	5.2
53.0	3.9	3.3	3.1	2.9	2.7	2.3		**71.0**	8.7	7.4	7.0	6.5	6.1	5.2
53.5	4.0	3.4	3.2	3.0	2.8	2.4		**71.5**	8.9	7.5	7.1	6.6	6.2	5.3
54.0	4.1	3.5	3.3	3.1	2.9	2.5		**72.0**	9.0	7.6	7.2	6.7	6.3	5.4
54.5	4.2	3.6	3.4	3.2	2.9	2.5		**72.5**	9.1	7.7	7.3	6.8	6.4	5.5
55.0	4.3	3.7	3.5	3.2	3.0	2.6		**73.0**	9.2	7.9	7.4	6.9	6.5	5.5
55.5	4.4	3.8	3.5	3.3	3.1	2.6		**73.5**	9.4	8.0	7.5	7.0	6.5	5.6
56.0	4.6	3.9	3.6	3.4	3.2	2.8		**74.0**	9.5	8.1	7.6	7.1	6.6	5.7
56.5	4.7	4.0	3.7	3.5	3.3	2.8		**74.5**	9.6	8.2	7.7	7.2	6.7	5.8
57.0	4.8	4.1	3.8	3.6	3.4	2.9		**75.0**	9.7	8.2	7.8	7.3	6.8	5.8
57.5	4.9	4.2	3.9	3.7	3.4	2.9		**75.5**	9.8	8.3	7.9	7.4	6.9	5.9
58.0	5.1	4.3	4.0	3.8	3.5	3.1		**76.0**	9.9	8.4	7.9	7.4	6.9	5.9
58.5	5.2	4.4	4.2	3.9	3.6	3.1		**76.5**	10.0	8.5	8.0	7.5	7.0	6.0
59.0	5.3	4.5	4.3	4.0	3.7	3.2		**77.0**	10.1	8.6	8.1	7.6	7.1	6.1
59.5	5.5	4.6	4.4	4.1	3.8	3.3		**77.5**	10.2	8.7	8.2	7.7	7.2	6.1
60.0	5.6	4.8	4.5	4.2	3.9	3.4		**78.0**	10.4	8.8	8.3	7.8	7.2	6.2
60.5	5.7	4.9	4.6	4.3	4.0	3.4		**78.5**	10.5	8.9	8.4	7.8	7.3	6.3
61.0	5.9	5.0	4.7	4.4	4.1	3.5		**79.0**	10.6	9.0	8.4	7.9	7.4	6.4
61.5	6.0	5.1	4.8	4.5	4.2	3.6		**79.5**	10.7	9.1	8.5	8.0	7.5	6.4
62.0	6.2	5.2	4.9	4.6	4.3	3.7		**80.0**	10.8	9.1	8.6	8.1	7.5	6.5
62.5	6.3	5.4	5.0	4.7	4.4	3.8		**80.5**	10.9	9.2	8.7	8.1	7.6	6.5
63.0	6.5	5.5	5.2	4.8	4.5	3.9		**81.0**	11.0	9.3	8.8	8.2	7.7	6.6
63.5	6.6	5.6	5.3	5.0	4.6	4.0		**81.5**	11.1	9.4	8.8	8.3	7.7	6.7
64.0	6.7	5.7	5.4	5.1	4.7	4.0		**82.0**	11.2	9.5	8.9	8.4	7.8	6.7
64.5	6.9	5.9	5.5	5.2	4.8	4.1		**82.5**	11.3	9.6	9.0	8.4	7.9	6.8
65.0	7.0	6.0	5.6	5.3	4.9	4.2		**83.0**	11.4	9.6	9.1	8.5	7.9	6.8
65.5	7.2	6.1	5.7	5.4	5.0	4.3		**83.5**	11.5	9.7	9.2	8.6	8.0	6.9
66.0	7.3	6.2	5.9	5.5	5.1	4.4		**84.0**	11.5	9.8	9.2	8.7	8.1	6.9
66.5	7.5	6.4	6.0	5.6	5.2	4.5		**84.5**	11.6	9.9	9.3	8.7	8.2	7.0

*Less than 85 cm should be measured lying down with height board.

Weight for Height Table Boys and Girls (49cm-130cm) continued

WEIGHT-FOR-HEIGHT							WEIGHT-FOR-HEIGHT						
			Malnutrition							Malnutrition			
			Moderate Wasting 70 to 79%		Severe Wasting <70%					Moderate Wasting 70 to 79%		Severe Wasting <70%	
Height (cm)	100% in Kg	85% in Kg	80% in Kg	75% in Kg	70% in Kg	60% in Kg	Height (cm)	100% in Kg	85% in Kg	80% in Kg	75% in Kg	70% in Kg	60% in Kg
85.0	12.0	10.2	9.6	9.0	8.4	7.2	**107.5**	17.7	15.0	14.1	13.3	12.4	10.6
85.5	12.1	10.3	9.7	9.1	8.5	7.3	**108.0**	17.8	15.2	14.3	13.4	12.5	10.7
86.0	12.2	10.4	9.8	9.1	8.5	7.3	**108.5**	18.0	15.3	14.4	13.6	12.7	10.8
86.5	12.3	10.5	9.8	9.2	8.6	7.4	**109.0**	18.1	15.4	14.5	13.6	12.7	10.9
87.0	12.4	10.6	9.9	9.3	8.7	7.4	**109.5**	18.3	15.6	14.6	13.7	12.8	11.0
87.5	12.5	10.6	10.0	9.4	8.8	7.5	**110.0**	18.4	15.7	14.8	13.8	12.9	11.0
88.0	12.6	10.7	10.1	9.5	8.8	7.6	**110.5**	18.6	15.8	14.9	14.0	13.0	11.2
88.5	12.8	10.8	10.2	9.6	8.9	7.7	**111.0**	18.8	16.0	15.0	14.1	13.1	11.3
89.0	12.9	10.9	10.3	9.7	9.0	7.7	**111.5**	18.9	16.1	15.1	14.2	13.3	11.3
89.5	13.0	11.1	10.4	9.7	9.1	7.8	**112.0**	19.1	16.2	15.3	14.3	13.4	11.5
90.0	13.1	11.1	10.5	9.8	9.2	7.9	**112.5**	19.3	16.4	15.4	14.4	13.5	11.6
90.5	13.2	11.2	10.6	9.9	9.2	7.9	**113.0**	19.4	16.5	15.5	14.6	13.6	11.6
91.0	13.3	11.3	10.7	10.0	9.3	8.0	**113.5**	19.6	16.7	15.7	14.7	13.7	11.8
91.5	13.4	11.4	10.8	10.1	9.4	8.0	**114.0**	19.8	16.8	15.8	14.8	13.8	11.9
92.0	13.6	11.6	10.8	10.2	9.5	8.2	**114.5**	19.9	16.9	16.0	15.0	14.0	11.9
92.5	13.7	11.6	10.9	10.3	9.6	8.2	**115.0**	20.1	17.1	16.1	15.1	14.2	12.1
93.0	13.8	11.7	11.0	10.3	9.7	8.3	**115.5**	20.3	17.3	16.2	15.2	14.2	12.2
93.5	13.9	11.8	11.1	10.4	9.7	8.3	**116.0**	20.5	17.4	16.4	15.4	14.3	12.3
94.0	14.0	11.9	11.2	10.5	9.8	8.4	**116.5**	20.7	17.6	16.5	15.5	14.5	12.4
94.5	14.2	12.0	11.3	10.6	9.9	8.5	**117.0**	20.8	17.7	16.7	15.6	14.6	12.5
95.0	14.3	12.1	11.4	10.7	10.0	8.6	**117.5**	21.0	17.9	16.8	15.8	14.7	12.6
95.5	14.4	12.2	11.5	10.8	10.1	8.6	**118.0**	21.2	18.0	17.0	15.9	14.9	12.7
96.0	14.5	12.4	11.6	10.9	10.2	8.7	**118.5**	21.4	18.2	17.1	16.1	15.0	12.8
96.5	14.7	12.5	11.7	11.0	10.3	8.8	**119.0**	21.6	18.4	17.3	16.2	15.1	13.0
97.0	14.8	12.6	11.8	11.1	10.3	8.9	**119.5**	21.8	18.5	17.4	16.4	15.3	13.1
97.5	14.9	12.7	11.9	11.2	10.4	8.9	**120.0**	22.0	18.7	17.6	16.5	15.4	13.2
98.0	15.0	12.8	12.0	11.3	10.5	9.0	**120.5**	22.2	18.9	17.8	16.7	15.5	13.3
98.5	15.2	12.9	12.1	11.4	10.6	9.1	**121.0**	22.4	19.1	17.9	16.8	15.7	13.4
99.0	15.3	13.0	12.2	11.5	10.7	9.2	**121.5**	22.6	19.2	18.1	17.0	15.8	13.6
99.5	15.4	13.1	12.3	11.6	10.8	9.2	**122.0**	22.8	19.4	18.3	17.1	16.0	13.7
100.0	15.6	13.2	12.4	11.7	10.9	9.4	**122.5**	23.1	19.6	18.4	17.3	16.1	13.9
100.5	15.7	13.3	12.6	11.8	11.0	9.4	**123.0**	23.3	19.8	18.6	17.5	16.3	14.0
101.0	15.8	13.5	12.7	11.9	11.1	9.5	**123.5**	23.5	20.0	18.8	17.6	16.5	14.1
101.5	16.0	13.6	12.8	12.0	11.2	9.6	**124.0**	23.7	20.2	19.0	17.8	16.6	14.2
102.0	16.1	13.7	12.9	12.1	11.3	9.7	**124.5**	24.0	20.4	19.2	18.0	16.8	14.4
102.5	16.2	13.8	13.0	12.2	11.4	9.7	**125.0**	24.2	20.6	19.4	18.2	16.9	14.5
103.0	16.4	13.9	13.1	12.3	11.5	9.8	**125.5**	24.4	20.8	19.6	18.3	17.1	14.6
103.5	16.5	14.0	13.2	12.4	11.6	9.9	**126.0**	24.7	21.0	19.7	18.5	17.3	14.8
104.0	16.7	14.2	13.3	12.5	11.7	10.0	**126.5**	24.9	21.2	19.9	18.7	17.5	14.9
104.5	16.8	14.3	13.4	12.6	11.8	10.1	**127.0**	25.2	21.4	20.1	18.9	17.6	15.1
105.0	16.9	14.4	13.6	12.7	11.9	10.1	**127.5**	25.4	21.6	20.4	19.1	17.8	15.2
105.5	17.1	14.5	13.7	12.8	12.0	10.3	**128.0**	25.7	21.8	20.6	19.3	18.0	15.4
106.0	17.2	14.6	13.8	12.9	12.1	10.3	**128.5**	26.0	22.1	20.8	19.5	18.2	15.6
106.5	17.4	14.8	13.9	13.1	12.2	10.4	**129.0**	26.2	22.3	21.0	19.7	18.4	15.7
107.0	17.5	14.9	14.0	13.1	12.3	10.5	**129.5**	26.5	22.5	21.2	19.9	18.6	15.9
							130.0	26.8	22.8	21.4	20.1	18.7	16.1

Weight for Height Table for Adolescent Boys

TABLE 2- ADOLESCENT BOYS

Adolescent Boys 130.5 cm to 146.cm (18yrs). Weight for Height Reference Table

Height (cm)	MEDIAN	Target weight	Moderate wasting W/H 70 to 79 %		Severe wasting W/H< 70 %		Height (cm)	MEDIAN	Target weight	Moderate wasting W/H 70 to 79 %		Severe wasting W/H< 70 %	
	100%	85%	80%	75%	70%	60%		100%	85%	80%	75%	70%	60%
130.5	27.2	23.1	21.8	20.4	19.0	16.3	147.0	37.9	32.2	30.3	28.4	26.5	22.7
131.0	27.5	23.3	22.0	20.6	19.3	16.5	147.5	38.3	32.5	30.6	28.7	26.8	23.0
131.5	27.8	23.6	22.2	20.9	19.5	16.7	148.0	38.6	32.8	30.9	29.0	27.0	23.2
132.0	28	23.8	22.4	21.0	19.6	16.8	148.5	39.0	33.1	31.2	29.3	27.3	23.4
132.5	28.3	24.1	22.6	21.2	19.8	17.0	149.0	39.3	33.4	31.4	29.5	27.5	23.6
133.0	28.6	24.3	22.9	21.5	20.0	17.2	149.5	39.7	33.7	31.8	29.8	27.8	23.8
133.5	28.9	24.6	23.1	21.7	20.2	17.3	150.0	40.0	34.0	32.0	30.0	28.0	24.0
134.0	29.2	24.8	23.4	21.9	20.4	17.5	150.5	40.4	34.3	32.3	30.3	28.3	24.2
134.5	29.5	25.1	23.6	22.1	20.7	17.7	151.0	40.8	34.7	32.6	30.6	28.6	24.5
135.0	29.9	25.4	23.9	22.4	20.9	17.9	151.5	41.1	35.0	32.9	30.8	28.8	24.7
135.5	30.2	25.6	24.2	22.7	21.1	18.1	152.0	41.5	35.3	33.2	31.1	29.1	24.9
136.0	30.5	25.9	24.4	22.9	21.4	18.3	152.5	41.9	35.6	33.5	31.4	29.3	25.1
136.5	30.8	26.2	24.6	23.1	21.6	18.5	153.0	42.3	35.9	33.8	31.7	29.6	25.4
137.0	31.1	26.4	24.9	23.3	21.8	18.7	153.5	42.6	36.2	34.1	32.0	29.8	25.6
137.5	31.4	26.7	25.1	23.6	22.0	18.8	154.0	43.0	36.6	34.4	32.3	30.1	25.8
138.0	31.8	27.0	25.4	23.9	22.3	19.1	154.5	43.4	36.9	34.7	32.6	30.4	26.0
138.5	32.1	27.3	25.7	24.1	22.5	19.3	155.0	43.8	37.2	35.0	32.9	30.7	26.3
139.0	32.4	27.6	25.9	24.3	22.7	19.4	155.5	44.2	37.6	35.4	33.2	30.9	26.5
139.5	32.7	27.8	26.2	24.5	22.9	19.6	156.0	44.6	37.9	35.7	33.5	31.2	26.8
140.0	33.1	28.1	26.5	24.8	23.2	19.9	156.5	45.0	38.3	36.0	33.8	31.5	27.0
140.5	33.4	28.4	26.7	25.1	23.4	20.0	157.0	45.4	38.6	36.3	34.1	31.8	27.2
141.0	33.8	28.7	27.0	25.4	23.7	20.3	157.5	45.8	38.9	36.6	34.4	32.1	27.5
141.5	34.1	29.0	27.3	25.6	23.9	20.5	158.0	46.2	39.3	37.0	34.7	32.3	27.7
142.0	34.4	29.3	27.5	25.8	24.1	20.6	158.5	46.7	39.7	37.4	35.0	32.7	28.0
142.5	34.8	29.6	27.8	26.1	24.4	20.9	159.0	47.1	40.0	37.7	35.3	33.0	28.3
143.0	35.1	29.8	28.1	26.3	24.6	21.1	159.5	47.5	40.4	38.0	35.6	33.3	28.5
143.5	35.5	30.1	28.4	26.6	24.9	21.3	160.0	48.0	40.8	38.4	36.0	33.6	28.8
144.0	35.8	30.4	28.6	26.9	25.1	21.5	160.5	48.4	41.1	38.7	36.3	33.9	29.0
144.5	36.1	30.7	28.9	27.1	25.3	21.7	161.0	48.8	41.5	39.0	36.6	34.2	29.3
145.0	36.5	31.0	29.2	27.4	25.6	21.9	161.5	49.3	41.9	39.4	37.0	34.5	29.6
145.5	36.9	31.3	29.5	27.7	25.8	22.1	162.0	49.8	42.3	39.8	37.4	34.9	29.9
146.0	37.2	31.6	29.8	27.9	26.0	22.3	162.5	50.2	42.7	40.2	37.7	35.1	30.1
146.5	37.6	31.9	30.1	28.2	26.3	22.6	163.0	50.7	43.1	40.6	38.0	35.5	30.4

Weight for Height Table for Adolescent Girls

TABLE 3- ADOLESCENT GIRLS

Adolescent Girls 130.5cm to 163.5cm (18 yrs). Weight for Height Reference Table

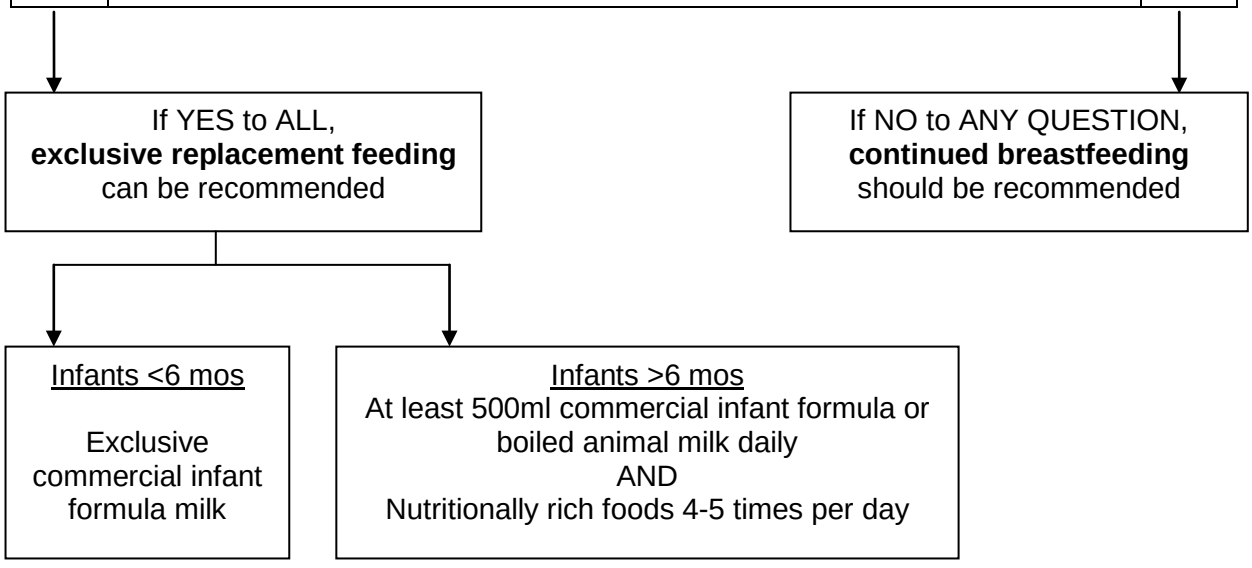
Height (cm)	MEDIAN	Target weight	Moderate wasting 70 to 79 %		Severe wasting < 70 %		Height (cm)	MEDIAN	Target weight	Moderate wasting 70 to 79 %		Severe wasting < 70 %	
	100%	85%	80%	75%	70%	60%		100%	85%	80%	75%	70%	60%
130.5	27.4	23.2	21.9	20.6	19.2	16.4	147.0	38.4	32.7	30.7	28.8	26.9	23.0
131.0	27.7	23.5	22.2	20.8	19.4	16.6	147.5	38.8	33.0	31.0	29.1	27.2	23.3
131.5	28.0	23.8	22.4	21.0	19.6	16.8	148.0	39.1	33.2	31.3	29.3	27.4	23.5
132.0	28.3	24.1	22.6	21.2	19.8	17.0	148.5	39.5	33.5	31.6	29.6	27.7	23.7
132.5	28.6	24.3	22.9	21.5	20.0	17.2	149.0	39.8	33.8	31.8	29.9	27.9	23.9
133.0	29.0	24.6	23.2	21.8	20.3	17.4	149.5	40.1	34.1	32.1	30.1	28.1	24.1
133.5	29.3	24.9	23.4	22.0	20.5	17.6	150.0	40.5	34.4	32.4	30.4	28.4	24.3
134.0	29.6	25.2	23.7	22.2	20.7	17.8	150.5	40.8	34.7	32.6	30.6	28.6	24.5
134.5	30.0	25.5	24.0	22.5	21.0	18.0	151.0	41.2	35.0	33.0	30.9	28.8	24.7
135.0	30.3	25.8	24.2	22.7	21.2	18.2	151.5	41.5	35.3	33.2	31.1	29.1	24.9
135.5	30.6	26.0	24.5	23.0	21.4	18.4	152.0	41.9	35.6	33.5	31.4	29.3	25.1
136.0	31.0	26.3	24.8	23.3	21.7	18.6	152.5	42.3	35.9	33.8	31.7	29.6	25.4
136.5	31.3	26.6	25.0	23.5	21.9	18.8	153.0	42.6	36.2	34.1	32.0	29.8	25.6
137.0	31.7	26.9	25.4	23.8	22.2	19.0	153.5	43.0	36.6	34.4	32.3	30.1	25.8
137.5	32.0	27.2	25.6	24.0	22.4	19.2	154.0	43.4	36.9	34.7	32.6	30.4	26.0
138.0	32.4	27.5	25.9	24.3	22.7	19.4	154.5	43.8	37.2	35.0	32.9	30.7	26.3
138.5	32.7	27.8	26.2	24.5	22.9	19.6	155.0	44.2	37.6	35.4	33.2	30.9	26.5
139.0	33.0	28.1	26.4	24.8	23.1	19.8	155.5	44.6	37.9	35.7	33.5	31.2	26.8
139.5	33.4	28.4	26.7	25.1	23.4	20.0	156.0	45.1	38.3	36.1	33.8	31.6	27.1
140.0	33.7	28.7	27.0	25.3	23.6	20.2	156.5	45.5	38.7	36.4	34.1	31.9	27.3
140.5	34.1	29.0	27.3	25.6	23.9	20.5	157.0	46.0	39.1	36.8	34.5	32.2	27.6
141.0	34.4	29.2	27.5	25.8	24.1	20.6	157.5	46.5	39.5	37.2	34.9	32.6	27.9
141.5	34.7	29.5	27.8	26.0	24.3	20.8	158.0	47.0	40.0	37.6	35.3	32.9	28.2
142.0	35.1	29.8	28.1	26.3	24.6	21.1	158.5	47.6	40.5	38.1	35.7	33.3	28.6
142.5	35.4	30.1	28.3	26.6	24.8	21.2	159.0	48.2	41.0	38.6	36.2	33.7	28.9
143.0	35.8	30.4	28.6	26.9	25.1	21.5	159.5	48.9	41.6	39.1	36.7	34.2	29.3
143.5	36.1	30.7	28.9	27.1	25.3	21.7	160.0	49.7	42.2	39.8	37.3	34.8	29.8
144.0	36.4	31.0	29.1	27.3	25.5	21.8	160.5	50.5	43.0	40.4	37.9	35.4	30.3
144.5	36.8	31.3	29.4	27.6	25.8	22.1	161.0	51.6	43.8	41.3	38.7	36.1	31.0
145.0	37.1	31.5	29.7	27.8	26.0	22.3	161.5	52.8	44.9	42.2	39.6	37.0	31.7
145.5	37.4	31.8	29.9	28.1	26.2	22.4	162.0	54.4	46.3	43.5	40.8	38.1	32.6
146.0	37.8	32.1	30.2	28.4	26.5	22.7	162.5	56.1	47.7	44.9	42.1	39.3	33.7
146.5	38.1	32.4	30.5	28.6	26.7	22.9	163.0	56.7	48.2	45.4	42.5	39.7	34.0
							163.5	56.7	48.2	45.4	42.5	39.7	34.0

Annex 20 Assessment for Safe Cessation of Breastfeeding: Children Under 12 Months

Given the high rate of malnutrition in Swaziland, and the associated morbidity and mortality, exclusive breastfeeding is recommended for the first 6 months of life. Breast milk, with the addition of nutritious complementary foods, should be provided thereafter until at least 12 months of age.

Some circumstances necessitate cessation of breastfeeding prior to 12 months. If a mother expresses the desire to stop breastfeeding early, the assessment below should be conducted. Only when ALL conditions for safe and nutritious breast milk alternatives are met can exclusive replacement feeding (ERF) be recommended.

YES	Assess the following conditions for safe cessation of breastfeeding	NO
	Is the child **healthy and growing** well (weight trend follows growth curve, W/H>100%)?	
	Are **safe water** and sanitation assured in the home and in the community?	
	Can the mother, or other caregiver, **afford and reliably provide** sufficient infant formula milk to support normal growth and development of the infant (about E500/month)?	
	Can the mother or caregiver **prepare formula milk cleanly** and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition?	
	If the infant is <6 months, can the mother or caregiver **exclusively** give infant formula?	
	Is the **family supportive** of exclusive replacement feeding?	
	Can the mother or caregiver **access health care** that offers comprehensive child health services?	



Annex 21 Assessment for safe cessation of breastfeeding for children 12 months and older

Mother is considering cessation of BF and child is at least 12 months old

YES	Assess the following conditions for safe cessation of breastfeeding	NO
	Is the child **healthy and growing** well (weight trend follows growth curve, W/H>100% and MUAC>12.5)?	
	Is the **family supportive** of discontinuation of breastfeeding?	
	Can the mother/caregiver **afford and/or reliably provide** at least 500ml milk daily (about E300/month or milk from a cow/goat, if available) to support normal growth and development of the child?	
	Are **nutritionally adequate alternative foods** (e.g. beans, greens, bananas, avocado, peanuts/peanut butter, eggs, meat) available and part of the regular diet?	
	Can the mother/caregiver **routinely provide 3 nutritious meals and 2 snacks** (milk can count as part of meal or snack)	
	Can the mother or caregiver **access health care** that offers comprehensive child health services?	

YES to ALL

Conduct **Rapid Test**

Rapid Test POSITIVE

- **Continue BFing**
- **Conduct DBS**
- Continue NVP (if eligible*)
- Continue CTX

DBS POSITIVE

- **Continue BFing**
- **Refer for ART**
- Stop NVP
- Continue CTX

DBS NEGATIVE

Rapid Test NEGATIVE

- Recommend **stop breastfeeding gradually** over one month
- Provide nutrition counselling
- Cont NVP (if eligible*) until 1week after BF cessation
- Give the child a 3m return appointment for **repeat HIV testing** (see EID algorithm) and growth monitoring
- Cont CTX until confirmed HIV negative after BF stops

Any NO answer

- **Continue BFing**
- Continue NVP (if eligible*)
- Continue CTX
- Provide advice to prepare for improved nutritional situation and routinely reassess
- Retest for HIV as per EID algorithm

*HIV-exposed children who are BFing are eligible for NVP if mother is not on ART.

Annex 22 Food Guide for HIV Exposed and Infected Infants and Children[30]

Age	Asymptomatic (10% more energy needed to maintain growth)	Symptomatic with no weight loss (20–30% more energy needed)	Symptomatic with weight loss (50–100% more energy needed)
0 – 6 months	Exclusive breastfeeding or exclusive replacement feeding at least 8 times/day	Exclusive breastfeeding or exclusive replacement feeding at least 8 times/day	Exclusive breastfeeding or exclusive replacement feeding at least 8 times/day
6 months	Introduction of solid foods: 2–3 tablespoons of energy-dense well-mashed or pureed foods twice a day	Introduction of solid foods: 2–3 tablespoons of energy-dense well-mashed or pureed foods twice a day	Introduction of solid foods: 3–4 tablespoons of energy-dense well- mashed or pureed foods twice a day
	Breastmilk or any kind of milk at least 8 times a day.	Breast milk or any kind of milk at least 8 times a day.	Breast milk or any kind of milk at least 8 times a day.
7 – 8 months	3-5 meals of ½ cup mashed high-energy, nutrient-dense foods from all food groups plus 1 energy-dense snack/d	5- 6 meals of 1/2 cup of mashed high-energy, nutrient-dense foods from all food groups plus 1 energy-dense snack a day	5 or 6 smaller, more frequent meals of ¼ to ½ cup of mashed food requiring less chewing with 1 or 2 snacks a day
	Continued breastfeeding or 1–2 cups of milk a day	Continued breastfeeding or 1–2 cups of any kind of milk a day	Continued breastfeeding or 1–2 cups of any kind of milk a day
9 - 11 months	Mashed or finely chopped foods that the infant can pick up	High-energy and nutrient-dense foods and all food groups	Foods that require less chewing or are easy to eat
	4 meals of ½-¾ cup mashed foods/day plus 1-2 energy-dense snacks between meals	4-5 meals of ½-¾ cup of mashed foods a day plus 1-2 energy-dense snacks between meals	5- 6 meals of ¾ cup of mashed foods/day plus 2-3 energy-dense snacks between meals
	Continued breastfeeding or 1–2 cups of milk a day	Continued breastfeeding or 1–2 cups of any kind of milk a day	Continued breastfeeding or 1–2 cups of any kind of milk a day
12 – 24 months	Mashed or chopped foods that the infant can pick up	High-energy and nutrient-dense foods and all food groups	Foods that require less chewing or are easy to eat
	4 meals of 1 cup of mashed foods a day plus 3 energy-dense snacks between meals	5 or 6 meals of 1 cup of mashed foods a day plus two energy-dense snacks between meals	6 to 8 small energy-dense meals of ¾ to 1 cup of foods a day plus 2 energy-dense snacks
	Continued breastfeeding or 1–2 cups of milk a day	Continued breastfeeding or 1–2 cups of any kind of milk a day	Continued breastfeeding or 1–2 cups of any kind of milk a day
	Adequate intake of clean boiled water	Adequate intake of clean boiled water	Adequate intake of clean boiled water

High energy, nutrient dense foods include margarine, butter, vegetable oil, dry milk powder, cooked eggs, cheese, ground nut paste, or fish powder.

[30] Adapted from "NUTRITION CARE FOR PEOPLE LIVING WITH HIV AND AIDS (PLWHA)", Regional Centre for Quality of Health Care, Uganda, 2008.

Annex 23 Preparing Animal Milk for Infants Under 6 Months

Health care practitioners occasionally come across infant feeding situations in which the mother has either died, is sick in the hospital, or is living apart from her child. While exclusive breastfeeding and formula feeding are the main two recommended feeding methods for infants younger than 6 months, in certain instances home modified animal milk can be used as a suitable replacement. Wet nursing is not recommended.

Preparing Modified Animal Milk for an Infant			
Infant's age	Milk Needed (cow milk, either fresh or UHT, or goat milk)	Water Needed	Sugar Needed
Birth to 1 month	40 ml	20 ml	1 level teaspoon
1 to 2 months	60 ml	30 ml	1 rounded teaspoon
3 to 4 months	80 ml	40 ml	2 level teaspoons
5 to 6 months	100 ml	50 ml	2 rounded teaspoons

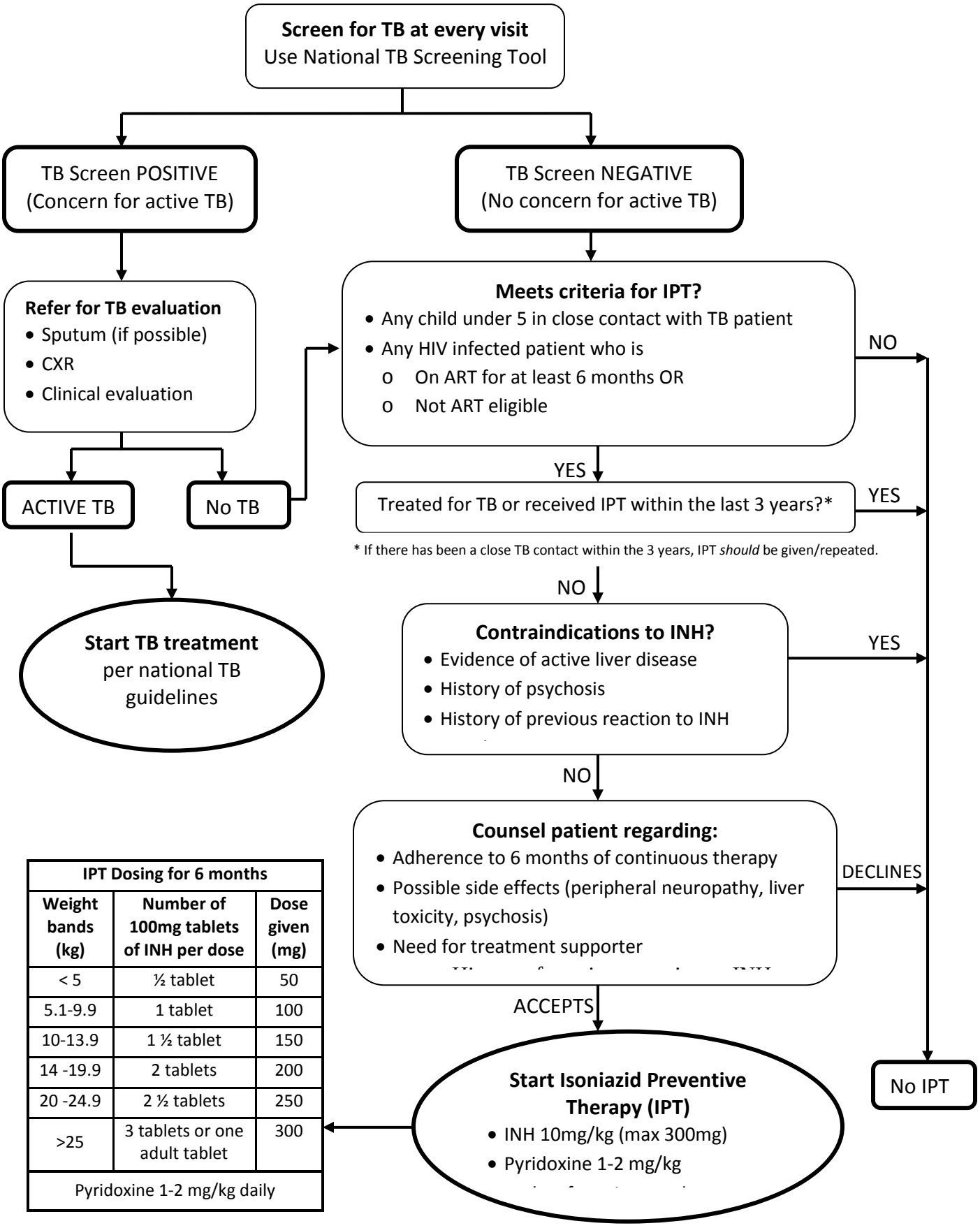
As babies grow older, they need more of the specially prepared cow's milk. The table below shows how many times a day a baby should be fed, how much the baby will need for each feed, and the total amount of milk needed per day. Some babies may eat more frequently than others, and some babies may eat less frequently, so this is just a guideline.

Amount of Milk Needed per Day			
Age	Feedings per Day	Volume of milk/feed	Volume of milk/day
Birth to 1months	8	60 ml	480 ml
1 to 2 months	7	90 ml	630 ml
2 to 4 months	6	120 ml	720 ml
4 to 6 months	6	150 ml	900 ml

The instructions for mixing fresh cow's milk need to be followed exactly. Adding too much or too little water can be dangerous for the baby. The infant does not need any water or any other types of liquids until it is six months old.

For additional instructions and patient guidance please see WHO brochure on "How to Feed Your Baby Fresh Cow's Milk."

Annex 24 Isoniazid (INH) Preventive Therapy Algorithm



IPT Dosing for 6 months		
Weight bands (kg)	**Number of 100mg tablets of INH per dose**	**Dose given (mg)**
< 5	½ tablet	50
5.1-9.9	1 tablet	100
10-13.9	1 ½ tablet	150
14 -19.9	2 tablets	200
20 -24.9	2 ½ tablets	250
>25	3 tablets or one adult tablet	300
Pyridoxine 1-2 mg/kg daily		

Annex 25 Tuberculosis Treatment Regimens for Children

Daily dosing is recommended based on the following dose in mg/kg body weight (range)

- Isoniazid (H) 5 mg/kg (4-6 mg/kg), maximum 300mg daily
- Rifampicin (R)10 mg/kg (8-12 mg/kg), maximum 600mg daily
- Pyrazinamide (Z) 25 mg/kg (20-30 mg/kg), maximum 2g daily
- Ethambutol* (E) 20 mg/kg (15-25 mg/kg), maximum 2.5g daily
- Streptomycin (S) 30mg/kg (20-40 mg/kg; under 1y, 20-30mg/kg), maximum 1g daily

Pyridoxine should be given at 1-2mg/kg (maximum 100mg) daily to prevent peripheral neuropathy

Category III TB Treatment Regimen for Children Under 8 Years

Weight (kg)	Intensive phase 2 months	Continuation phase 4 months			Pyridoxine 6 months (25mg)
	RHZ (60/30/150mg)	RH (60/30mg)	OR	RH (150/75mg)	
3-4 kg	½ tab	½ tab	OR	--	¼ tab
5-7 kg	1 tab	1 tab	OR	½ tab	½ tab
8-9 kg	1 ½ tabs	1 ½ tabs	OR	1 tab	½ tab
10-14 kg	2 tabs	2 tabs	OR	1 tab	½ tab
15-19 kg	3 tabs	3 tabs	OR	1½ tabs	1 tab
20-24 kg	4 tabs	4 tabs	OR	2 tabs	1 tab
25-29 kg	5 tabs	5 tabs	OR	2½ tabs	1 tab
30-35 kg	6 tabs	6 tabs	OR	3 tabs	1 tab

Category I TB Treatment Regimen for Children 8 Years and Older

Weight (kg)	Intensive phase 2 months	Continuation phase 4 months			Pyridoxine 6 months (25mg)
	RHZE (150/75/400/275mg)	RH (150/75mg)	OR	RH (300/150mg)	
13-19 kg	1 tab	1 tab	OR	½ tab	½ tab
20-29 kg	1 ½ tabs	1 ½ tabs	OR	--	1 tab
30-37 kg	2 tabs	2 tabs	OR	1 tab	1 tab
38-54 kg	3 tabs	3 tabs	OR	1½ tabs	1 tab
55-70 kg	4 tabs	4 tabs	OR	2 tabs	2 tabs
>71 kg	5 tabs	5 tabs	OR	2½ tabs	2 tabs

* Historically ethambutol was avoided in children below 8 years of age because of fears of ocular toxicity. Extensive review of the evidence suggests that these fears are overstated and ethambutol is now recommended for children with smear positive TB or severe forms of TB and those on re-treatment. The dosage of ethambutol should be strictly calculated by weight and close monitoring for loss of vision is necessary.

Annex 26 Adolescent Risk Assessment

There are many issues to consider when dealing with adolescents. Sexual development, peer pressure, school issues, increasing responsibilities, and denial can place an adolescent in a vulnerable position and lead to risk-taking behaviours. Disempowerment and abuse are unfortunately all too common. Orphaned adolescents may be forced to become leaders of the household, forcing many to turn to sex as a form of income generation.

Current and potential risk-taking behaviours need to be addressed and actively prevented on an ongoing basis. The screening tool below can be easily incorporated into routine adolescent visits.

HEADSS Assessment: A Screening Tool for High-Risk Behaviours and Depression in Adolescents		
	Domain	Questions
H	HOME	Is the home environment safe? Is it stable? Who is the adolescent's primary caregiver/support?
E	EDUCATION	Is the adolescent going to school? How is school performance?
A	ACTIVITIES	What does the adolescent do for fun?
D	DRUGS	Does the adolescent drink alcohol or use drugs?
S	SEX	Has the adolescent had sex before? Consensual or forced? Is s/he being pressured to have sex? Is s/he exchanging sex for money? Does s/he understand choices concerning safer sex? Is s/he empowered to exercise these choices? Does she need a family planning method?
S	SUICIDE	Is the adolescent depressed? Is s/he planning to commit suicide? Has s/he tried to commit suicide in the past?

Health care workers should explore these issues with the adolescent, or refer as appropriate. With an understanding of the adolescent's problems, the health care worker will be able to build an empathetic relationship with the adolescent to provide ongoing counselling and treatment support to encourage good follow-up and adherence.