Guidelines For The Clinical Management Of HIV Infection In Children

In Myanmar

THIRD EDITION

National AIDS Programme
Department Of Health, Ministry Of Health, Myanmar
2011

World Health Organization
Country Office for Myanmar

GUIDELINES
FOR THE CLINICAL MANAGEMENT OF HIV INFECTION IN CHILDREN IN MYANMAR

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Contents

List of Abbreviations

3TC	lamivudine
ABC	abacavir
AFB	acid-fast bacilli
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
a.m.	ante meridiem (denotes morning)
ANC	antenatal care
ART	antiretroviral therapy
ARV	antiretroviral (drug)
AST	aspartate aminotransferase
ATV	atazanavir
AUC	area under curve
AZT	zidovudine (also known as ZDV)
BAL	bronchoalveolar lavage
BCG	bacille Calmette – Guérin (vaccine)
BSA	body surface area
CD4+	T-lymphocyte bearing CD4 receptor
%CD4+	percent CD4+ Centers for
CDC	Disease Control and Prevention
CHAP	Children with HIV Antibody Prophylaxis (clinical trial)
CMV	cytomegalovirus
CNS	central nervous system
CPK	creatinine phosphokinase
CRAG	cryptococcal antigen
CSF	cerebrospinal fluid
CTX	co-trimoxazole
d4T	stavudine
DART	Development of Antiretroviral Therapy (in Africa)
DMPA	depot medroxyprogesterone acetate
DNA	deoxyribonucleic acid
DOT	directly observed therapy
EC	enteric-coated
EFV	efavirenz
EIA	enzyme immunoassay
EML	Essential Medicines List
ELISA	enzyme-linked immunosorbent assay
ETV	etravirine
EU	European Union
EWI	early warning indicator
FDC	fixed-dose combination
FPV	fos-amprenavir
FTC	emtricitabine
Grade	grading of recommendations assessment, development and evaluation
HDL Hgb	lipoprotein haemoglobin
HGC	hard gel capsule
HIV	human immunodeficiency virus
HIVDR	HIV drug resistance
HIVNET	HIV Network for Prevention Trials
HIVResNet	Global HIV Drug Resistance Network
HSV	herpes simplex virus
IDV	indinavir
IMCI	integrated management of childhood illness
INH	isoniazid
IPT	isoniazid preventive therapy

DBS	dried blood spot
ddI	didanosine
LDH	lactate dehydrogenaRT
LGE	lineal gingival erythema
LIP	lymphocytic interstitial Pneumonia
LPV	lopinavir
LTB	laryngotracheal bronchitis
MCH	maternal-child health
MDR	multidrug resistant
MTCT	mother-to-child transmission (of HIV)
MUAC	mid-upper arm circumference
NAT	nucleic acid amplification test
NFV	nelfinavir
NNRTI	non-nucleoside reverse transcriptase inhibitor
NPA	nasopharyngeal aspirate
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	non-steroidal anti-inflammatory drug
NVP	nevirapine
OI	opportunistic infection
PCP	Pneumocystis pneumonia
PCR	polymerase chain reaction
PENTA	Children's Fund Paediatric European Network for Treatment of AIDS
PGL	persistent generalized Lymphadenopathy
PI	protease inhibitor
p.m.	post meridiem (denotes afternoon)
PMTCT	prevention of mother-to-child transmission (of HIV)
/r	low-dose ritonavir
RCT	randomized controlled trial
RDA	recommended daily allowance
REE	resting energy expenditure
IRIS	immune reconstitution inflammatory syndrome
RNA	ribonucleic acid
RTI	reverse transcriptase inhibitor
RTV	ritonavir
RUTF	ready-to-use therapeutic feeds
SD	standard deviation
sd-NVP	single-dose nevirapine
SQV	saquinavir
T20	enfurvirtide
TAM	thymidine analogue mutation
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
TEN	toxic epidermal necrolysis
TLC	total lymphocyte count
TPV	tipranavir
TRG	Technical Reference Group on Paediatric HIV Care and Treatment
TST	tuberculin skin test
ULN	upper limit of normal
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations
Up24 Ag	ultrasensitive p24 antigen
URTI	upper respiratory tract infection
USAID	United States Agency for International Development
WBC	white blood cell count
WHO	World Health Organization
XD	Rextensively drug resistant

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Nay Pyi Taw, 2011

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Introduction

This is the third edition of the *Guidelines for the Management of HIV Infection in Children in Myanmar.* As in the second edition, published in 2007, this document is the result of a consultative approach. It is necessary to revise and update the previous guidelines to keep up with current changes in diagnosis and management of HIV infection in children.

Meetings of the guideline review committee were conducted in Naypyidaw and Yangon in March and April, 2011 to review and revise the previous second edition. During meetings, comments of users in the field were also taken into consideration. With the development of new standards for the quality of serological and virogical assays, earlier and more accurate diagnosis of HIV can be made. With earlier initiation of ART and simplified ARV for use in first line and second line therapy, outcome of HIV infected children and children born to HIV infected mothers have improved. World Health Organization (WHO) published an update revised HIV treatment guidelines, including *Antiretroviral therapy for HIV infection in infants and children towards universal access: Recommendations for a public health approach in 2010.* Our guidelines for the Management of HIV Infection in Children in Myanmar were updated by adapting and adopting the WHO recommendations.

These *Guidelines* will be useful for all medical professionals in Myanmar involved in the management of HIV/AIDS in children. The aim is to provide flexibility in the recommendations given to accommodate the different capacities of programs which are providing care to children in Myanmar. New drugs which are likely to become available during the 2-3 year were included in this guideline.

Significant changes made in this revised guidelines include the following:

- Earlier and more accurate diagnosis
- Earlier initiation of ART
- Simplified ARVs for use in first line and second line therapy
- Promoting attention to nutrition for children on ART
- Considerations for prevention and treatment of infants and children with tuberculosis and HIV.
- New emphasis on Pneumocystis jerovesi pneumonia prophylaxis for all children born to HIV-infected mother and older HIV infected children
- New recommendations on PMCT and infant feeding practices.

The *Guidelines* do not replace textbooks and publications and do not provide complete information. This guideline give guidance adapted to resource-constrained settings.

The *Guidelines* are at a level consistent with the constraints of existing health and social services in Myanmar. Information is presented as structured decision steps allowing symptoms and infections to be readily identified and managed. This information complements the health care professional's own clinical judgment. These *Guidelines* aim to be applicable to State/Division, District and Township level hospitals in Myanmar.

1. Diagnosis of HIV infection in children

Although HIV testing is currently widely available in the country, children born to HIV-infected mothers are often not identified at the time of birth. The mother's HIV status is also often unknown. This situation may change with increasing detection of HIV-exposed children due to expansion of PMCT programs. Usually, children infected with HIV are first diagnosed clinically. Subsequently, HIV testing is performed for the child as well as the mother. Clinical recognition of the signs and symptoms of HIV infection in children is important for early diagnosis, counselling and testing for the infant and family.

Clinical Diagnosis

Clinical recognition of symptomatic HIV infection in children

Clinical recognition of symptomatic HIV infection in children is made if the following are present.[1]

- Any **cardinal** finding:
  - Pneumocystis carinii pneumonia (PCP)
  - Lymphoid interstitial pneumonitis (LIP), a chronic lung disorder of unknown cause that affects up to 40% to 50% of perinatally HIV-infected children. Epstein-Barr virus (EBV) and HIV itself have been identified in biopsy specimens from children with LIP.
  - Fungal infection in throat and mouth (candidiasis or thrush)
- Two or more **characteristic** findings:
  - Recurrent bacterial and/or viral infections (such as respiratory infections, skin infections and meningitis)
  - Tuberculosis of the lung or of other organs
  - Shingles (herpes zoster)
  - Cytomegalovirus infection
  - Neurological problems, such as slowness in developing skills in sitting, crawling and talking, fits and microencephaly (reduced head growth)
- One characteristic findings plus two or more **associated** findings:
  - Oral thrush when the child is not being treated with antibiotics
  - Failure to thrive (lack of weight gain)
  - Fever (continuous or intermittent for more than 1 month)
  - Diarrhoea (persistent or intermittent for more than 14 days)
  - Generalized lymphadenopathy (swollen lymph glands)
  - Skin rashes
- Three or more associated findings plus any **epidemiological risk factors**:
  - Mother has tested positive for HIV
  - History of transfusion of unscreened blood or blood products
  - Use of contaminated syringes and needles or a history of scarification, ear piercing or circumcision using non-sterile instruments
- Two associated findings plus **laboratory evidence** of HIV infection in the child.

The diagnosis of paediatric HIV infection is likely if at least two major and at least two minor signs are present. These clinical case definitions are limited by its low sensitivity and HIV testing is recommended whenever possible.

Major signs

1. weight loss or abnormally slow growth
2. chronic diarrhoea (>1 month)
3. prolonged fever (>1 month)

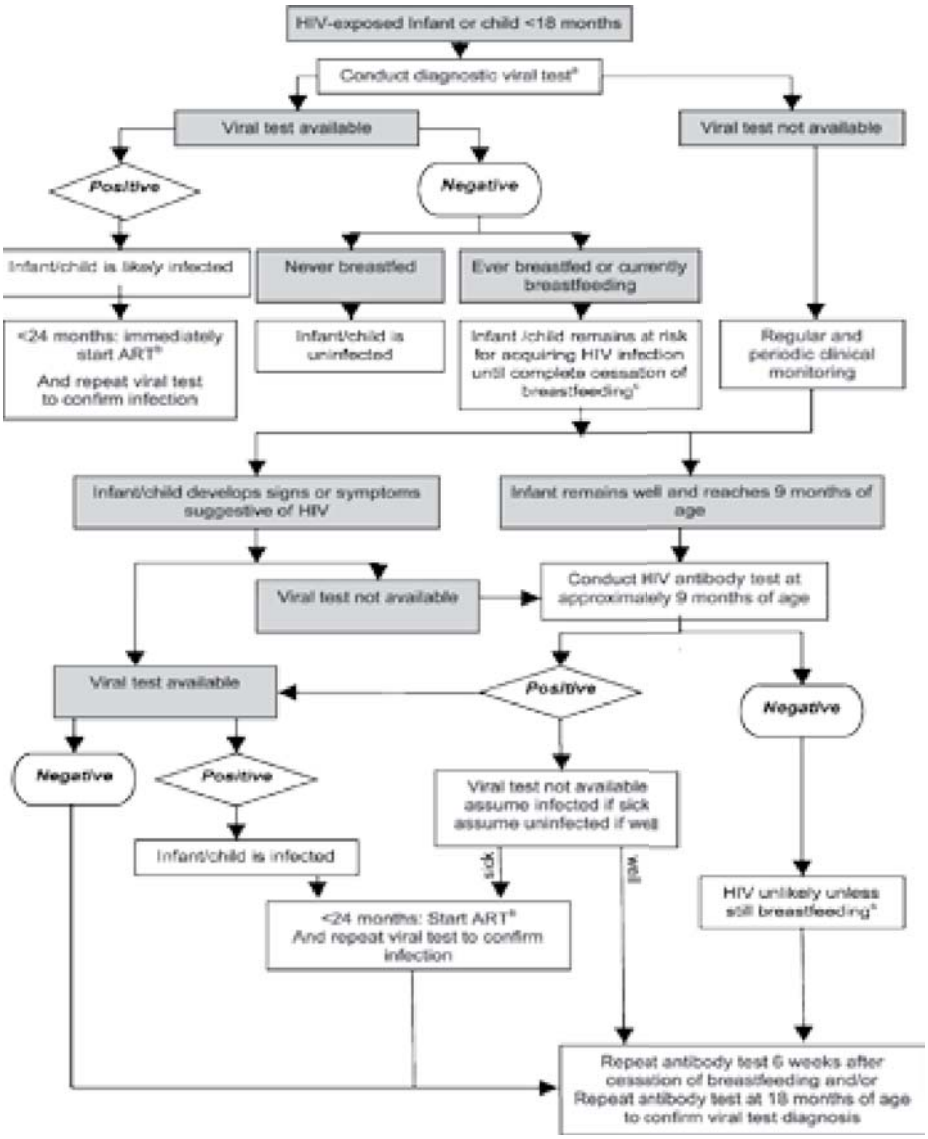
Minor signs

1. Generalized lymph node enlargement
2. Oro-pharyngeal candidiasis
3. Recurrent common infections, such as ear infection, pharyngitis, persistent cough
4. Generalized rash
5. Confirmed HIV infection in the mother

Laboratory Diagnosis of HIV infection in children[2]

1. HIV serological testing will be used as a diagnostic assay for children aged 18 months or older. Every initial positive antibody assay requires confirmation with a 2nd test using a different assay technique
2. If HIV virological testing is available, it will be used to diagnose HIV infection in infants and children less than 18 months of age.
3. Well infants born to HIV infected mother should have HIV serological testing at around 9 months of age (at the time of last immunization visit) and if reactive, should have a virological testing if available to identify infected infants who need ART. If virological testing is not available, repeat serological testing at 18 months of age.
4. In sick infants in whom HIV infection is being considered as an underlying cause of symptoms and signs, and virological testing is not available, HIV serological testing will be performed and the clinical algorithm for presumptive clinical diagnosis of HIV infection will be used for management. If available, HIV virological testing is to be done to confirm the diagnosis.
5. A breast feeding infant or child is at risk for acquiring HIV infection throughout the entire breast feeding period. Breast feeding should not be stopped in order to perform any kind of diagnostic HIV test. A positive virological test results should be considered to reflect HIV infection, and the usual confirmatory algorithms followed. However, interpreting negative results is difficult. A six-week window period after the complete cessation of breastfeeding is advised before testing; only then can negative virological test results be assumed to reliably rule out HIV infection. This applies to breastfeeding infants and children of all ages.

Fig 1 .Establishing the presence of HIV infection in HIV-exposed infants and Children less than 18 months of age.[2]



a. For newborn , test first at or around birth or at the first postnatal visit (usually 4-6 weeks)
b. Start ART, if indicated, without delay. At the same time, retest to confirm infection.
c. The risk of HIV transmission remains as long as breastfeeding continues.

Figure 2. Establishing the presence of HIV infection in sick infants and children less than 18 months of age where viral testing is available[2]

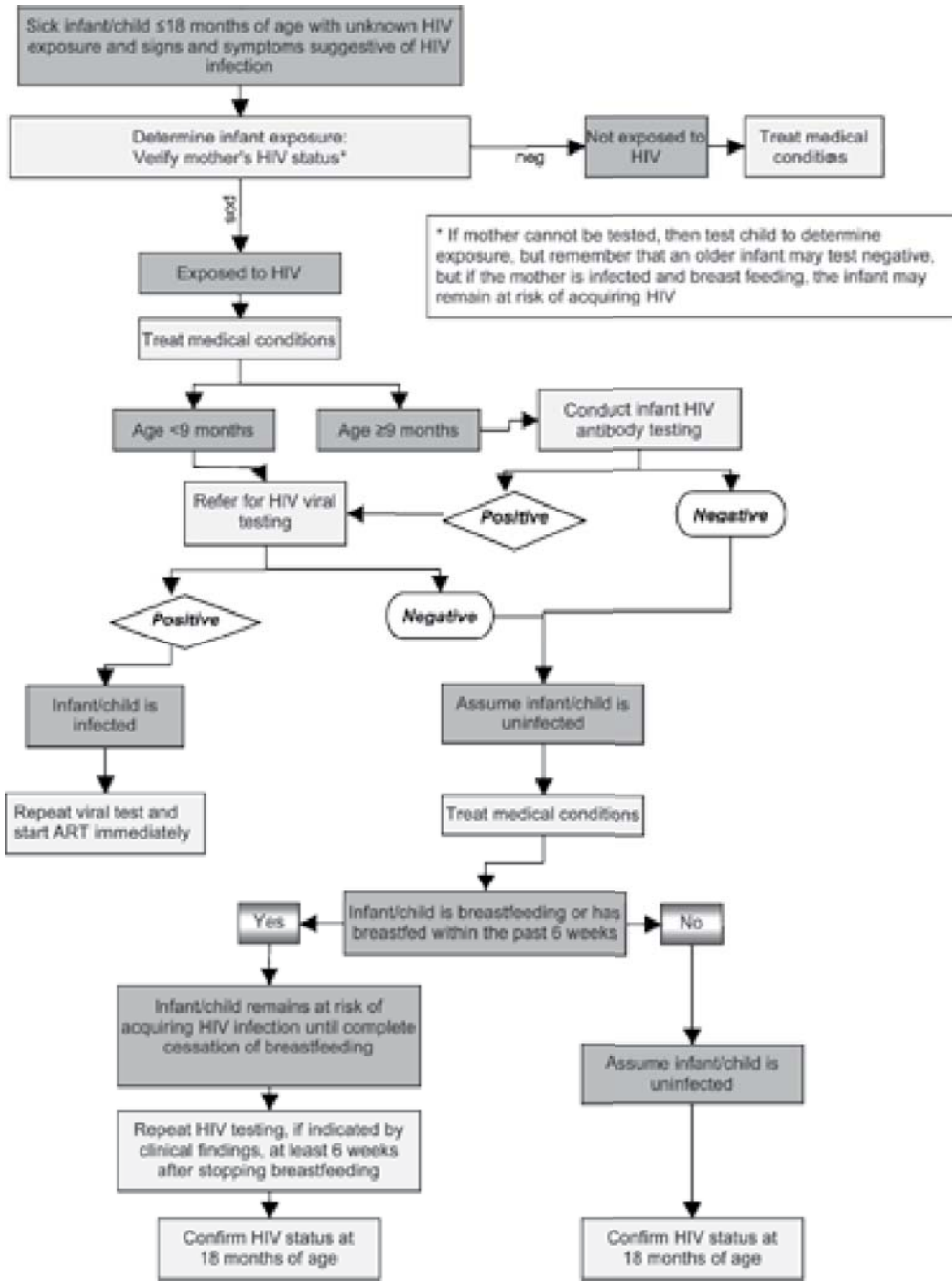
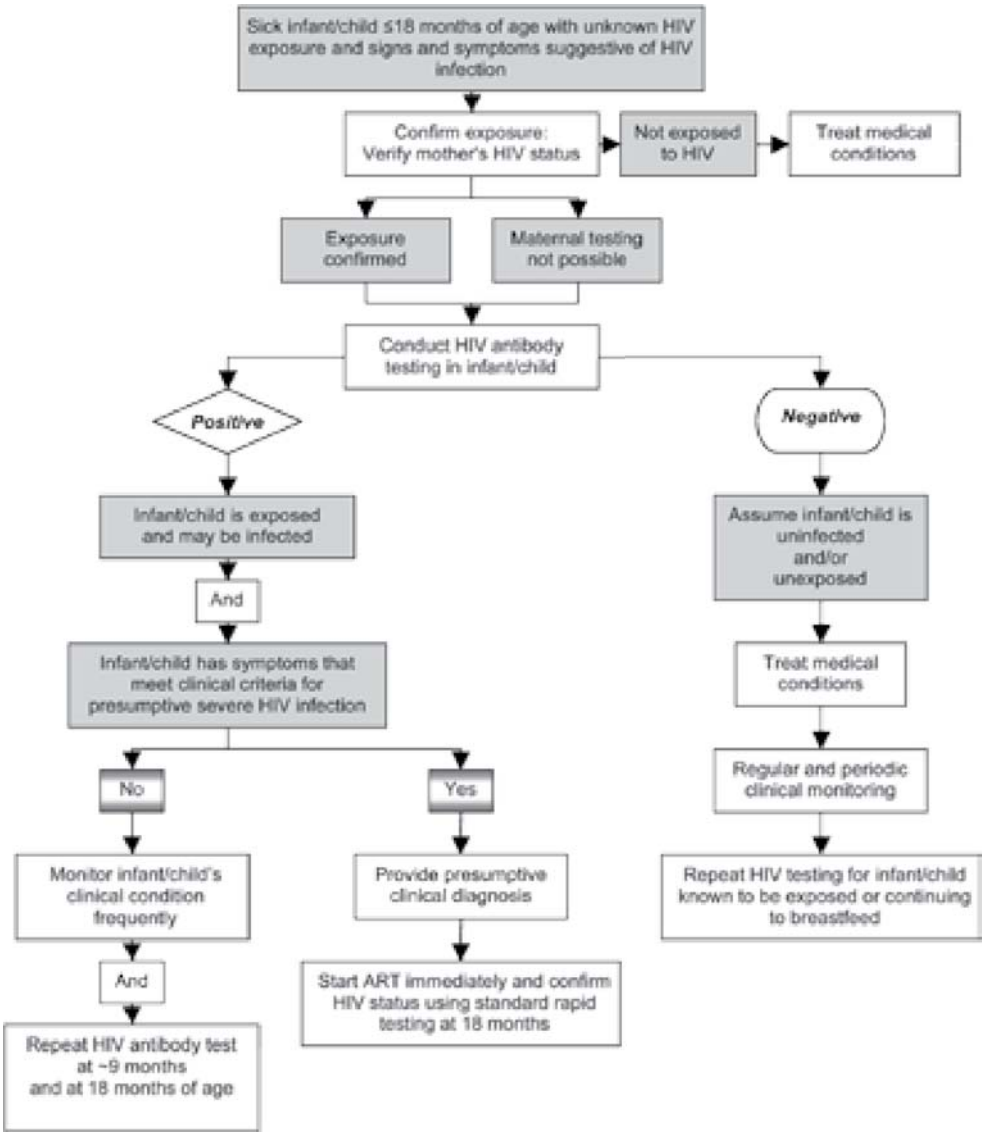


Figure 3. Establishing the presence of HIV infection in sick infants and children less than 18 months of age where viral testing is not available[2]



2. Management of children born to HIV- infected mothers

The ultimate goal of caring for these children is to maintain health by providing access to comprehensive care and support services. Comprehensive care includes antiretroviral therapy for treatment of established HIV infection and for the prevention of perinatal transmission of HIV, in addition to the prevention (prophylaxis) and treatment of opportunistic infections, counselling and testing, psycho-social and nutritional support.

Infant feeding counselling [3,4,5,6]

Explain risk of HIV transmission through breastfeeding and implications of mixed feeding. Specifically, explain that mixed feeding results in more HIV transmission than exclusive breastfeeding.

- Ensure mothers and family members understand the need to balance the competing risks of reducing the risk of HIV to infants through breastfeeding with the need for minimising the risk of other causes of morbidity and mortality through not breastfeeding
- Provide counselling and information about the risks and benefits of various infant feeding options based on locally feasible and acceptable feeding practices
- Recommend avoidance of all breast feeding and should only give commercial infant formula milk as a replacement feed to their HIV uninfected infants or infants who are of unknown HIV status, when specific conditions needed to safely formula feed are met.

NOTE: For HIV-negative women and women who do not know their status

Counselling should be performed in the context of protection and promotion of exclusive breastfeeding and support for 6 months, then introducing nutritionally adequate and safe complementary foods with continued breastfeeding for up to two years of age or beyond for women whose HIV status is unknown and women who are not infected with HIV.

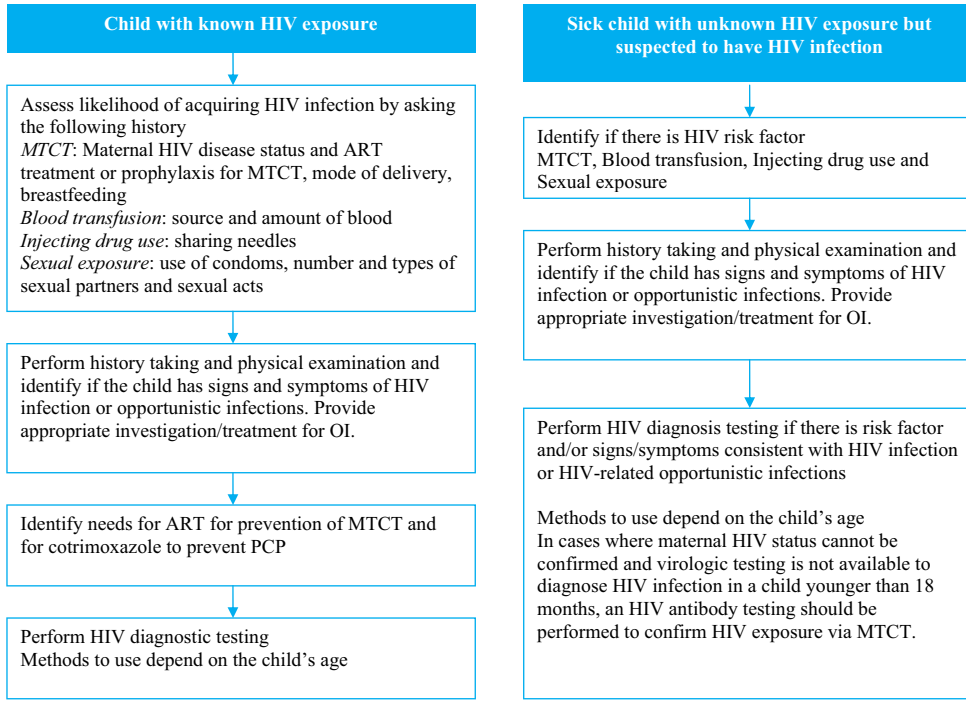
Family education, counselling and support

- Good hygienic practice:
  - do not allow pets inside house
  - drink boiled water
- How to prevent horizontal spreading of HIV-infection. Casual household contacts are safe.
- Appropriate infant feeding
- Advice on appropriate activities according to age group, including going to school
- Identify what the family needs and provide or refer to appropriate support

- Provide moral support, promote family values, love and caring, counsel and intervene in cases of domestic violence
- Involve family in caring for the child

Table (1) Assessment and management at the first visit

Child with known HIV exposure or a sick child with unknown HIV exposure but suspected to have HIV infection [7]



Notes:

- Maternal advanced HIV disease and low CD4 are risk factors for HIV transmission
- Successful treatment with ART in mothers lower the chance of transmission
- HIV transmission can occur via breastfeeding. A child remains at risk for HIV acquisition as long as he/she is breastfed.

3. HIV staging in children using clinical and immunological criteria

Table(2) HIV staging in children using clinical criteria

WHO classification of HIV-associated clinical disease	
Classification of HIV-associated clinical disease	**WHO Clinical Stage**
Asymptomatic	1
Mild	2
Advanced	3
Severe	4

Table (3) HIV staging in children using immunological Criteria (CD4)

WHO classification of HIV-associated immunodeficiency using CD4				
Classification of HIV-associated immunodeficiency	**Age-related CD4 values**			
	< 11 months (%)	**12 - 35 months(%)**	**36-59 months(%)**	**≥ 5 years (cells/mm^3)**
Not significant	> 35	> 30	> 25	> 500
Mild	30 - 35	25 - 30	20 - 25	350−499
Advanced	25 - 30	20−25	15−20	200−349
Severe	<25	<20	<15	<200 *or* <15%

Table (4) HIV staging in children using immunological Criteria (TLC)[12]

Classification of HIV-associated immunodeficiency	**Age-related TLC values**			
	< 11 months (cells/mm^3)	**12 - 35 months (cells/mm^3)**	**36-59 months (cells/mm^3)**	**≥ 5 years (cells/mm^3)**
Severe	<4000	<3000	<2500	<2000

Notes:

- Clinical staging in children without ART can predict mortality; however, it is heavily dependent on the presence of malnutrition. Clinical staging is used as a guide for cotrimoxazole and ART management particularly in situations where CD4 is not available.

- CD4 is the best measurement for assessing immune deficiency. CD4 should be used in conjunction with clinical assessment; however, CD4 allows an earlier detection of worsening of HIV disease as CD4 decline usually occurs before there is clinical progression. CD4 monitoring can aid in the decision to initiate or switch ART. Younger children normally have higher CD4 than older children and adults. CD4% varies less in children < 6 years old and is the preferred measurement. At age ≥ 6 years, either CD4% or CD4 count can be used. The threshold CD4 levels for severe immunodeficiency in children age 1 year and up corresponds with a 12 month mortality risk of ≤ 5%. In children younger than 1 year and especially < 6 months, CD4 is less predictive of mortality and there is high risk for death even at high %CD4.

- Total lymphocyte count (TLC) is only used if CD4 measurement is not available and it should only be used to categorize severe immune suppression. Calculation of TLC = % lymphocyte X total white blood cell count.

- The predictive value of lymphocytes count should not be used for the evaluation of response to ART, because a change in TLC is a poor predictor of treatment success.

4. Cotrimoxazole prophylaxis forPneumocystis jirovecii Pneumonia (PCP)

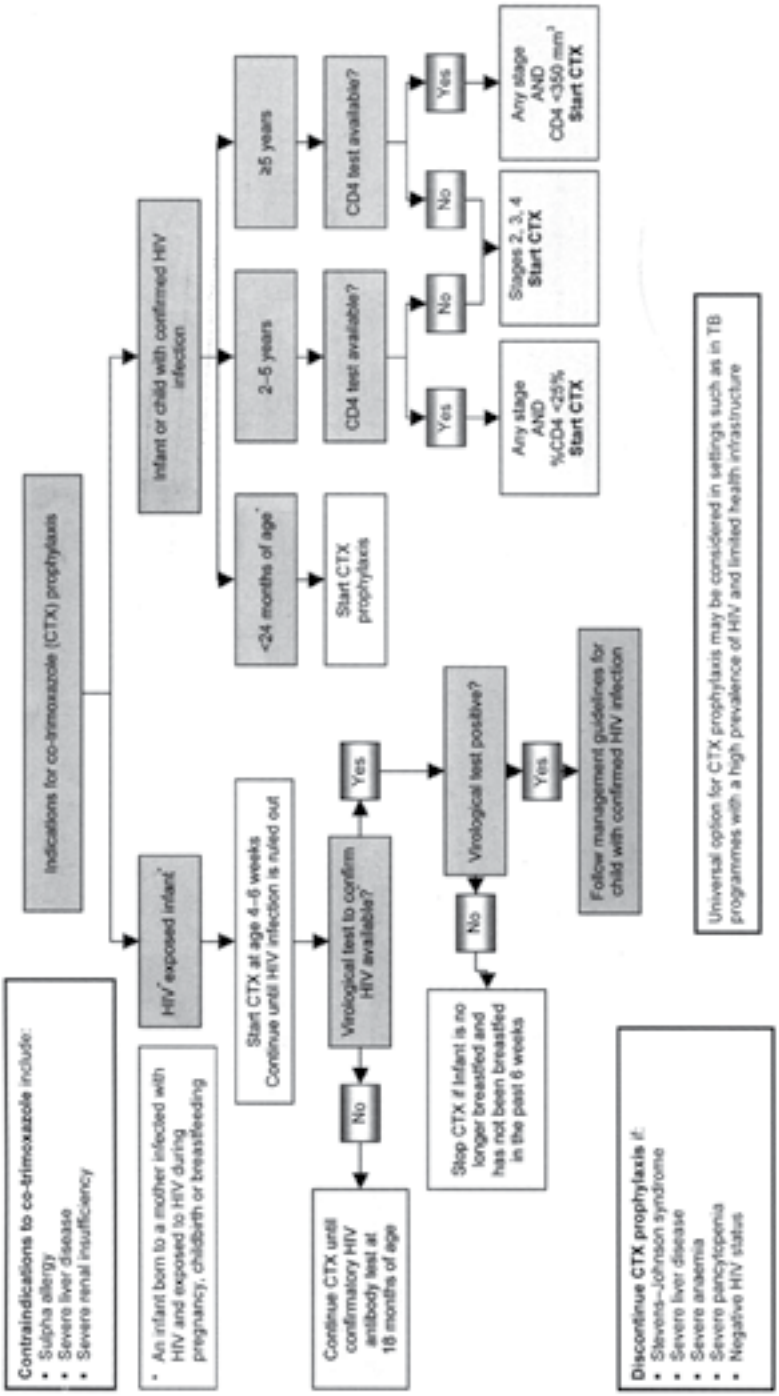


Figure 4 Initiating co-trimoxazole prophylaxis [2]

Notes:

α Defined as a child born to an HIV-infected mother or child breastfeeding from an HIV-infected mother until HIV exposure stops (6 weeks after complete cessation of breast feeding) and infection can be excluded

β In children under 18 months HIV infection can only be confirmed by virological testing.

χ Once started on CTX should continue until 5 years regardless of clinical symptoms or CD4 %. Specifically, infants who begin CTX prophylaxis before the age of one year and who subsequently are asymptomatic and/or have CD4 levels ≥ 25% should remain on CTX prophylaxis until they reach 5 years of age.

HIV-exposed infants and children [8]

Cotrimoxazole prophylaxis is recommended for all HIV-exposed infants starting at 4–6 weeks of age (or at first encounter with the health care system) and continued until HIV infection can be excluded. Cotrimoxazole is also recommended for HIV-exposed breastfeeding children of any age and cotrimoxazole prophylaxis should be continued until HIV infection can be excluded by HIV antibody testing (beyond ≥ 18 months of age) or virological testing (< 18 months of age). The risk of PCP is greatest in the first 6 months of life.

Infants and children with documented HIV-infection

All children under two years of age with **documented** HIV infection should receive cotrimoxazole prophylaxis regardless of symptoms or CD4 percentage. Beyond the age of two years, initiation of cotrimoxazole prophylaxis is recommended for symptomatic children (WHO stages 2, 3 or 4) or children with CD4 <25%.[1] All children who commence cotrimoxazole prophylaxis (irrespective of whether cotrimoxazole was initiated in the first two years of life) should continue until the age of five years when they can be reassessed. Adult clinical staging and CD4 count thresholds for cotrimoxazole initiation or discontinuation apply for children older than five years of age.[9]

In children with **presumptive symptomatic** HIV disease, cotrimoxazole prophylaxis should be started at any age and continued until HIV infection status can be excluded.

Children in whom cotrimoxazole prophylaxis is contraindicated

Children with a history of severe adverse reactions (Stevens-Johnson Syndrome) to cotrimoxazole or other sulpha drugs, severe liver disease and severe renal insufficiency should not be prescribed cotrimoxazole prophylaxis. In resource limited settings, routine testing for G6PD deficiency is not recommended. Dapsone 2mg/kg once daily, if available, is an alternative. Some children will be intolerant to both cotrimoxazole and dapsone. No alternative recommendation can be made in the context of resource limited settings in children who are intolerant to both.

Discontinuation of cotrimoxazole prophylaxis

If there is severe adverse reactions (Stevens - Johnson syndrome), severe liver disease, severe anaemia, severe pancytopenia developed and if negative HIV status can be confirmed.

Table (5) Doses of cotrimoxazole in infants and children

Recommended daily dosage [a]	Suspension (5 ml syrup 200 mg /40 mg)	Paediatric tablet (100 mg/20 mg)	Single strength adult tablet (400 mg/ 80 mg)	Double strength adult tablet (800 mg/160 mg)
< 6 months 100 mg SMX /20 mg TMP	2.5 ml	One tablet	¼ tablet, possibly mixed with feeding [b]	----
6 months – 5 years 200 mg SMX /40 mg TMP	5 ml [c]	Two tablets	Half tablet	----
> 6 – 14 years 400 mg SMX /80 mg TMP	10 ml [c]	Four tablets	One tablet	Half tablet
> 14 years 800 mg SMX/ 160 mg TMP	----	----	Two tablets	One tablet
Frequency - once a day				

Notes:

a) Some counties may use weight bands to determine dosing. Age and corresponding weight bands are

Age	Weight
<6 months	<5 kg
6 months-5 years	5-15 kg
6–14 years	15-30 kg
>14 years	>30 kg

b) Splitting tablets into quarters is not considered best practice. This should be done only if syrups are not available.

c) Children of these ages (6 months -14 years) may be able to swallow crushed tablets.

Secondary cotrimoxazole prophylaxis in infants and children

Children with a history of treated PCP should be administered secondary cotrimoxazole prophylaxis with the same regimen recommended for primary prophylaxis.[10]

5. Immunization schedule forHIV-exposed or HIV-infected children

Table (6) Recommended immunization schedule for HIV-exposed or HIV-infected children

Vaccine	Age							
Vaccine	At Birth	1 Month	1 1/2 Months	2 1/2 Months	3 1/2 Months	6 Months	9 Months	18 months
Tuberculosis	BCG							
Diphtheria, pertussis, tetanus			DPT1	DPT2	DPT3			
Polio			OPV1	OPV2	OPV3			
Measles						Measles1	Measles2	Measles3
Hepatitis B	HBV1		HBV2		HBV3			

Notes: [11]

- BCG is recommended at birth for all babies born to HIV infected mothers.
- BCG is contraindicated in children with proved HIV-infection status.
- Either IPV or OPV can be used.
- All the optional vaccines are considered according to feasibility and affordability.

6. Management of HIV-infected children

For HIV-infected children, comprehensive care involves support for the child and family with appropriate measures to prevent, diagnose and treat opportunistic infections and the use of antiretroviral therapy.

- Assess the growth and nutritional status, and need for intervention
- Assess the immunization status and provide appropriate immunizations
- Assess for signs and symptoms of OIs and history of exposure to TB. If an OI is suspected, diagnosis and treatment of the OI takes priority over initiation of ART.

- Assign the WHO clinical stage
- Ensure that the child is on co-trimoxazole
- Identify concomitant medications that may produce drug interactions with ART
- Stage HIV disease using immunological criteria
- Perform a CD4 count if available
- CD4% is preferred in children <5 years and CD4 count is preferred in children ≥5 years

- To calculate the CD4% and count, a full blood cell count (FBC) needs to be performed (ideally automated)

- Assess whether the child fulfils the criteria for starting ART
- Proper counseling is important for treatment adherence because non-adherence to treatment is the main reason for treatment failure.
- Starting ART is not an emergency but once started the treatment must be given on time everyday.
  Non – adherence to treatment is the main reason for treatment failure.
- Assess the family situation including, but not limited to, the number of persons with or at risk for HIV infection and their current health/treatment status.
- Identify the primary caregiver for the child and his/her ability and willingness to adhere to follow-up schedules and treatment for HIV, especially ART.
- Identify other caregivers who may be responsible for administering ART.
- Assess family members' understanding of HIV disease and its treatment.
- Assess the disclosure status of HIV diagnosis within the family (whether the child knows his/her diagnosis, whether anyone else knows, and if the child knows the parent[s]' HIV status).
- Assess the financial status of the family, including their ability to pay for transportation to the clinic, afford adequate food/nutritional supplements for the child, pay for any treatment needed and whether they have a refrigerator for keeping ARVs that need to be stored at a low temperature, if required.

7. Starting ART

Conditions necessary to introduce antiretroviral therapy

- Access to functioning and affordable health services and support networks into which ARV treatment can be integrated so that the treatments are provided effectively
- Information and training on safe and effective use of ARVs for health professionals in a position to prescribe ARVs
- Capacity to diagnose HIV infection and to diagnose and treat concomitant illnesses.
- Assurance of adequate supply of quality drugs
- Sufficient resources should be identified to pay for treatment on a long term basis; patients must be aware that treatment is 'for life'
- Functioning laboratory services for monitoring including routine haematological and biochemical tests to detect toxicities, must be available
- Access to voluntary HIV counselling and testing (VCT) and follow up counselling services should be assured, including counselling on the necessity of adherence to treatment.

Starting ART using clinical and CD4 criteria [2]

Table (7) Recommendations for initiating ART in infants and children; revised in 2010

Age	Infants and children <24 months of age a,b	≥24 months of age to 59months of age	Five years of age or older
%CD4+	All[c]	≤25	NA
Absolute CD4	All[c]	≤750 cells/mm3	≤350 cells/mm^3 (As in adults)

(a) All HIV-infected infants should receive ART due to the rapid rate of disease progression.
(b) Countries with reliable access to CD4 monitoring may choose to apply clinical and immunological criteria for initiation of ART in children aged 12 – 23 months
(c) In children with absolute lymphopaenia, the CD4 percentage (%CD4+) may be falsely elevated.

Table (8) : Recommendations for initiating ART in HIV-infected infants and children according to clinical stage and immunological markers

	Clinical stage	Immunological
<24 months	Treat all	
>24 months	Stage 4[a]	Treat all[b]
	Stage 3[a]	Treat all
	Stage 2	Treat if CD4 below age-adjusted threshold Don't treat if no CD4 available:
	Stage 1	

(a) Stabilize any opportunistic infection (OI) before initiating ART.
(b) Baseline CD4 is useful for monitoring ART even if it is not required to initiate ART.

Criteria for starting ART in infants and children less than 18 months with a presumptive diagnosis of severe HIV disease [2]

Where access to virological testing is not yet available, criteria for making a presumptive diagnosis of severe HIV disease in children less than 18 months of age developed by WHO can be used in order to allow initiation of potentially life-saving ART. Any presenting acute illnesses should be managed first followed by prompt initiation of antiretroviral therapy.

In infants and children who have been started on ART on the basis of a presumptive diagnosis of severe HIV disease, treatment should be closely monitored and confirmation of HIV infection should be obtained as soon as possible using age-appropriate testing methods. Additionally, HIV serological testing should be performed at 18 months of age to confirm definitive HIV infection status in the child. Decisions on further treatment should be adjusted at that time in accordance with the results. ART should be stopped in infants and children only where HIV infection can be confidently ruled out and when such children are no longer exposed to HIV (i.e. through breastfeeding from an HIV-infected mother).

The initiation of ART on the basis of a presumptive diagnosis of severe HIV disease is not recommended for use by providers who are not appropriately trained in HIV care or the administration of ART. Presumptive diagnosis of severe HIV disease should not be used in children aged 18 months and older as antibody testing establishes their HIV infection status.

Table (9): Criteria for presumptive diagnosis of severe HIV disease in infants and children <18 months of age where viral testing is not available

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. A diagnosis of any AIDS-indicator condition(s) [A] can be made

Other findings that support the diagnosis of severe HIV disease in an HIV-seropositive infant include:
– Recent HIV-related maternal death or advanced HIV disease
– Child's %CD4+ <20%

Confirm the diagnosis of HIV infection as soon as possible.

[A] - AIDS indicator conditions include some but not all HIV paediatric clinical stage 4 conditions such as Preumocystis Pneumonia, cryptococcal meningitis, severe wasting or severe malnutrition , Kaposi Sarcoma, extrapulmonary TB.

8. Recommended first line ART regimens[2]

Infants and children <24 months

The recommended first-line regimen for infants and children <24 months with no prior exposure to maternal or infant NNRTIs, or whose exposure to maternal or infant ARVs is unknown, is to start standard NVP-containing triple therapy.

Box 1 : Preferred regimen for NVP-naïve infants or children <24 months with no known prior exposure to NVP
NVP + 3TC + AZT

Two NRTIs are combined with NVP as the NNRTI (Box 1). Reverse transcriptase inhibitor drugs prevent HIV replication by inhibition of the action of reverse transcriptase, the enzyme that HIV uses to make a DNA copy of its RNA. EFV is not currently recommended for use in children less than 3 years of age due to lack of information on appropriate dosing.

Box 2 : Preferred initial regimen for NNRTI- exposed infants or children <24 months
LPV/r + 3TC + AZT

While the guidelines panel felt the evidence and risk – benefit analysis warranted the above recommendation to be strong, they also recognized that in many resource-limited settings, LPV/r is not available, affordable or, due to cold chain requirements, not feasible for use. It is also acknowledged that the use of LPV/r in a first-line regimen may compromise the potential to construct a potent second- line regimen.

Children ≥24 months

The recommended first-line regimen for HIV-infected children ≥24 months of age, is two NRTIs plus one NNRTI (Box 1). There are two exceptions: the use of EFV should be avoided in adolescent girls (due to the teratogenic potential of EFV in the first trimester of pregnancy) and in children less than 3 years of age (due to lack of appropriate dosing information in this age group). See Table (10) for a summary of recommended first-line ART regimens for infants and children.)

The use of a triple NRTI regimen (i.e. [AZT or d4T] + 3TC + ABC) can be considered as an option for initial therapy in special circumstances (see Box 3). Of concern is the somewhat lower virological potency of this regimen compared with a two-class triple-drug combination in adult studies. Currently, a triple NRTI regimen is only recommended in children less than three years of age who are receiving treatment for TB, a situation where NVP may not be an optimal choice because of drug interactions with rifampicin. This regimen could be considered for adolescents who may become pregnant, or adolescents with anticipated or documented poor adherence.

Box 3: Recommended alternative ARV regimen for infants and children to simplify management of toxicity, co morbidity and drug-drug interaction
AZT or d4T[a] + 3TC[b] + ABC

(a) AZT should not be given in combination with d4T.
(b) FTC can be used instead of 3TC in children more than 3 months of age.

Table (10) Summary of preferred first-line ARV regimens for infants and children

Patient group	Standard first-line regimen
Infants	
Infant or child <24 months not exposed to ARVs	NVP + 2 NRTI
Infant or child <24 months exposed to NNRTI	LPV/r + 2 NRTI
Infant or child <24 months with unknown ARV exposure	NVP + 2 NRTI
Children	
Children 24 months to 3 years	NVP + 2 NRTI
Children >3 years	NVP or EFV + 2 NRTI

Box 4 Nevirapine-based regimens
Nevirapine + AZT/3TC (preferred) OR Nevirapine + ABC/3TC OR Nevirapine + d4T/3TC

Box 5 Efavirenz-based regimens
Efavirenz + AZT/3TC (preferred) OR Efavirenz + ABC/3TC OR Efavirenz + d4T/3TC

Box 6: Protease inhibitor-based regimens
Lopinavir/ritonavir + AZT/3TC (preferred) OR Lopinavir/ritonavir + ABC/3TC OR Lopinavir/ritonavir + d4T/3TC

Box 7: Preferred first-line regimens for specific situations	
Situation	**Preferred first-line regimen**
CONCOMITANT CONDITIONS	
Child or adolescent with severe anaemia	NVP + 2 NRTIs (avoid AZT)
Child <3 years with TB treatment	NVP + 2 NRTIs OR 3 NRTIs: AZT or d4T + (3TC + ABC)
Child >3 years or adolescent with TB treatment	EFV + 2 NRTIs OR 3 NRTIs: AZT or d4T + (3TC + ABC)
Adolescent with hepatitis B	TDF + FTC or 3TC + NNRTI*

9. Immune reconstitution inflammatory syndrome (IRIS)

Definition	A collection of signs and symptoms resulting from the ability to mount an immune response associated with immune recovery on ART.[13]
Frequency	10% of all patients initiating ART Up to 25% among patients initiating ART with a CD4 cell count < 50.[14 15]
Timing	Typically within 2-12 weeks of initiation of ART but may present later
Signs and symptoms	Unexpected deterioration of clinical status soon after commencing ART Unmasking of subclinical infections such as TB, which present as new active disease Worsening of co-existing infections such a flare of hepatitis B or C
Most common IRIS events	60% of IRIS events are M.Tuberculosis MAC or Cryptococcal disease[16]
Management	• IRIS may be mild and resolve without treatment. • Continue ART if the patient can tolerate it. • Treat unmasked active OI, such as TB. This may mean temporary interruption of ART until the patient is stable on TB drugs, then reintroduction of ART. • Consider other causes for the child's symptoms, including drug reaction (NVP, EFV, cotrimoxazole • Corticosteroid treatment to suppress exaggerated inflammatory response may be indicated. For example, an acute hepatic flare where viral hepatitis coinfection is known or suspected. • Prednisone 0.5-1.0 mg/kg/day for 5-10 days is suggested in moderate to severe cases of IRIS.[17]

Notes:

- IRIS presents as an unexpected deterioration in clinical condition with signs and symptoms of inflammation/infection soon after commencing ART
- Typically 2-12 weeks
- **It does not mean ART is failing**
- It is a paradoxical reaction against a foreign antigen (alive or dead) in patients who have started ART and have undergone a reconstitution of their immune responses against this antigen. MTB accounts for approx. 1/3 of all IRIS events.

Management Principles

- Continue ART if possible
- Discontinue ART and prioritize treatment of the pathogen in patients who are severely unwell
- Treat the specific pathogen in order to decrease the antigen load
- Consider corticosteroids in moderate to severe cases of IRIS
- Prednisolone (or prednisone) at (0.5-1.0 mg/kg/day)
- orally or IV for five to ten days or longer depending on the severity of the inflammation
- Discontinue ART and prioritize treatment of the pathogen in patients who are severely unwell
- Aspiration and drainage of lymph nodes and abscesses (may need to be repeated several times)
- Emergency surgical decompression in cases of trachea or intestinal obstruction.

10. Adherence assessment and strategies to improve adherence

Children are not small adults, especially in relation to the assessment and support of adherence. Adapted approaches and tools are necessary and should be available and understood by health care personnel. In order to do so, a comprehensive knowledge of the various factors and constraints that influence adherence is essential: factors related to the child itself, the caretaker, the health care provider, the regimen factors and the society in general. Support and assessment of adherence in children is a continuous procedure, starting well in advance of treatment and throughout further follow up. Depending on the stage, whether preparing for treatment or already taking ARV drugs, different issues need to be addressed and adapted approaches applied.

Table 11: Specific issues to be addressed in supporting adherence in children

Preparation before starting ARV	While on ARV treatment
Related to the child	
How to communicate and evaluate the readiness? • Communication on health, sickness, pain, treatment and adherence issues can be done through fairy tails and games. Depending on the child's maturity, it can include other issues like treatment plan, treatment monitoring, disclosure and transmission routes. • Any communication should be open and fair, enabling the child to express feelings and to ask questions, whether individually or in groups. • The message should be clear and positive focussing on "AIDS can be treated". • Disclosure should not a prerequisite for good adherence. However, the issue can be addressed through tools.	Communication and evaluation • Plays need to be an integral part of ARV clinics. This helps the children to live positively with HIV/AIDS, provides fun and is a perfect way to provide information, education and communication • Communication can happen individually but also in groups, allowing children to share experiences without compulsory disclosure, e.g., a child shows how he/she swallows tablets. • The importance of adherence is crucial during further follow up and can be addressed through different games and fairy tales. • An evaluation of the child's worries and feelings is essential to adherence, especially at the commencement of treatment.

. • Assessment of readiness requires proximity in order to sense the child's perspective towards treatment but also to evaluate the willingness / ability to swallow medicines. Swallowing of pills can be taught (starting with smaller pills, see swallowing protocol); alternatives can be found (crushing and mixing of tablets, opening of some capsule, use of syrup). • Prophylactic drugs can be used as a tool to assess adherence prior to starting HAART	• Adherence assessment can be done through various ways: o open and direct questioning o pill counting o self report of child (e.g. through drawing, stickers in diary) o assessing the understanding of given information • The limitations of adherence assessment should be acknowledged with the focus on support for unconditional adherence from the very beginning. • Tools for adherence support (e.g., diary for self reporting)

Related to the caretaker	
The role of the caretaker is crucial • Identification of a caretaker and evaluation of his/her relationship with the child is a prerequisite • The caretaker should understand and accept his responsibility for all doses of the child's medication Communication with the caretaker should address: o the caretaker's attitude towards HIV/AIDS o caretakers expectations towards HAART o all caretakers unanswered questions that might lead to stress or isolation of the child o essential issues like HIV transmission, AIDS can be treated, children can grow, and the importance of adherence o basic knowledge on OI and ARV treatment • Any HIV-infected caretaker should be part of a family-centred model of care and treatment: ARV should be provided if needed.	• Caretakers should join the children's activities and can apply tools themselves to communicate with their child. • Communication between caretaker and health care provider should take place in a friendly relationship. This can take place in individual sessions but also through group counselling. • Group counselling offers problem sharing and support from peers. • Evaluate the needs and feelings of the caretaker. Other problems, different from the child's health, might be a priority. • The crucial role of the caretaker in ensuring adherence should be acknowledged at every visit. Tools to support adherence (reminders, pill boxes) should be provided to child and caretaker.

Related to the regimen	

• Use a child friendly regimen.
  ○ paediatric formulations should be available, e.g., syrups, smaller tablets or even paediatric fixed dose combinations
  ○ allow children's preference for adult formulations (tablets, capsules)
  ○ learn which adult formulations can be divided and mixed, e.g., some capsules can be opened
  ○ use maximum twice daily dosage
  ○ take palatability into account
  ○ teach child and caretaker how to improve taste e.g., by mixing with juice
• Provide knowledge on possible toxicities to caretaker and on appropriate self-management
• The child should always be able to see the pills prior to regimen selection
	• Integrate intake of medicines with pleasant daily activities
	  ○ e.g., link with tooth brushing, favourite TV program
	• Provide tools to remind (funny pill boxes), to express positive/negative feelings (e.g., drawings), to visualize prescription (sticker of medicines and dosage) and to award intake (e.g., stickers)
	• Offer proximity to health care provider, e.g., hotline in case of toxicities

Related to health care provider	

• Communication tools (fairy tales and games to improve knowledge of caretaker and child, to address adherence issues) and tools to assess and support adherence should be available for the provider.
• Address attitude and create understanding for provider by improving their knowledge:
  ○ on HIV pathogenesis
  ○ rational of HAART
  ○ importance of adherence, including the message “HIV-infected children can grow, can live normal lives, can attend schools, …”
	• Promote a multidisciplinary approach by team working involving doctors, nurses, social workers, pharmacists and PHAs

11. Clinical and Laboratory Monitoring of HIV infected Children [2]

The efficacy of combined antiretroviral therapy is indicated by an improvement of clinical and to a certain extent laboratory markers of HIV infection. Clinical criteria that give some indication of response to treatment should be monitored closely. Laboratory parameters that give some indication of response to treatment should be monitored according to the judgment of the treating physician. Clinical and laboratory data is detailed in the outpatient department (OPD) card as well as in the log book. Define outcome data to be collected and monitor outcome data on a regular basis.[1]

Baseline clinical assessment for children

Following confirmation of HIV infection status, the baseline clinical assessment for children should include:

- weight, height, head circumference and other measures of growth
- clinical staging of HIV disease (Annex 1)
- developmental status
- screening for malaria, TB disease, and exposure to TB
- identification of concomitant medical conditions (e.g. hepatitis B or C infection, TB, other co infections or OIs, pregnancy in adolescent girls)
- details of concomitant medications, including co-trimoxazole and traditional or herbal therapies
- nutritional status, including assessment of the quality and quantity of intake
- for those eligible for ART, assessment of the child's and caregiver's preparedness for therapy.

Baseline laboratory assessment for children

- Confirmation of HIV infection using virological or antibody testing.
- Measurement of CD4 % (preferable for children < 5 years) or absolute CD4 count where available.
- Haemoglobin measurement where AZT containing first-line regimens are being used.
- White blood cell count (WBC), if available.
- Pregnancy test, if indicated from the history, for sexually active adolescent girls.
- Hepatitis B and C status, where available.
- Viral Load where available.

Routine monitoring of children who are not yet eligible for ART

- Because of the rapid rate of disease progression in infants and young children, more frequent clinical and laboratory monitoring is indicated for them than for adults. The clinical evaluation of HIV – infected children who are not yet eligible for ART should be preformed every three to six months, at a minimum , and should include the same parameters as are used in the base line evaluation

Routine monitoring of children on ART

Once an infant or child is on ART, the frequency of clinical monitoring will depend on their response to ART. At a minimum, after starting ART, follow up visits should occur:

- For infants, at weeks 2, 4, 8 and then every 4 weeks for the first year.
- For children, at weeks 2, 4,8,12 and then every 2 to 3 months once the child has stabilized on therapy.

Routine clinical assessment should include addressing the child ‘s and/or care giver‘s understanding of and adherence to therapy , along with their need for additional support . Key signs of an infant‘s and child‘s response to ART include:

- Improvement in growth in infants and children who have been failing to grow.
- Improvement in neurological symptoms and development in children with encephalopathy or those who have demonstrated delay in the achievement of developmental milestones.
- Decreased frequency of infections (bacterial infections , oral thrush and/or other OIs)
- Observation of the child ‘s response to therapy should include vigilance for symptoms of potential drug toxicities or treatment failure. (i.e. – reassessment of WHO clinical stage)

Table 12: Laboratory parameters for monitoring infants and children at baseline, before and during ART

Laboratory test for diagnosis and monitoring	Baseline (at entry into care)	At initiating of first-line or second-line ART regimen	Every six months	As required or symptom directed
HIV diagnostic testing	✔			
Haemoglobin [a]	✔	✔		✔
WBC and differential count	✔	✔	✔	✔
%CD4+ or absolute CD4 cell count [b]	✔	✔	✔	✔
Pregnancy testing in adolescent girls		✔ [c]		✔ [d]
Full chemistry (including, but not restricted to, liver enzymes, renal function, glucose, lipids, amylase, lipase and serum electrolytes) [e]				✔
HIV VL measurement [g,f]				✔
OI screening (where possible)	✔			✔

(a) Haemoglobin monitoring at week 8 after initiation of ART is recommended if AZT is used.

(b) HIV-infected children not yet eligible for ART should be monitored with CD4 count every six months. For infants and children who develop new or recurrent WHO stage 2 or 3 events, or whose CD4 count approaches threshold values, the frequency of CD4 measurement can be increased.%CD4+ is preferred in children <5 years of age.

(c) Pregnancy testing may be needed for adolescent girls prior to initiating a regimen containing EFV.

(d) For pregnant adolescent girls, provide prophylaxis or combination ART to those who are in need of it for their own health and/ or to prevent vertical transmission. (See WHO PMTCT Guidelines, 2010)

(e) Routine monitoring (every six months) of full chemistry, particularly lipid levels, liver enzymes and renal function, should be considered for infants and children on second-line drugs.

(f) At present, VL measurement is not a prerequisite for initiation or regular monitoring of ART in resource-limited settings. VL can be used to diagnose HIV infection, and to confirm clinical or immunological failure prior to switching treatment regimen.

(g) VL should be assessed in infants on NNRTI-based regimens who are known to have been exposed to NNRTIs intrapartum or through breastfeeding.

12. Managing ARV toxicity[2]

Guiding principles in the management of ARV drug toxicity

1. Determine the seriousness of the toxicity.
2. Evaluate concurrent medications and establish whether the toxicity may be attributable to an ARV drug or drugs, or to a non-ARV medication taken at the same time.
3. Consider other disease processes (e.g. viral hepatitis in a child on ARV drugs who develops jaundice). Not all problems that arise during treatment are caused by ARV drugs.
4. Manage the adverse reaction according to its severity
   In general:
   (a) *Severe life-threatening reactions:* Immediately discontinue all ARV drugs, manage the medical event (i.e. provide symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized.[a]
   (b) *Severe reactions:* Substitute the offending drug without stopping ART. [a]
   (c) *Moderate reactions:* Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitution. [a]
   (d) *Mild reactions:* Reassure child and caregiver that while the reaction may be bothersome, it does not require a change in therapy; provide counselling and support to mitigate adverse reactions.
5. Stress the maintenance of adherence despite toxicity for mild and moderate reactions.

Substituting Drugs Because of Toxicity in Infants and Children

Principles

- Drug substitutions should be limited to situations where toxicity is severe or life-threatening, as there are few ARV options for children in resource-limited settings.
- If toxicity is related to an identifiable drug in a regimen, the offending drug can generally be replaced with another drug from the same class that does not have the same adverse effect.

Given the limited number of ARV drug options available in resource-limited settings, drug substitutions should only be considered when the toxicity is severe or life-threatening.

Table (13) lists the usual ARV substitution options for adverse reactions among the recommended combination first-line regimens. If toxicity is severe and seems clearly related to a specific drug, the offending drug can generally be replaced with another

from the same class that does not share the same type of toxicity, (e.g. substitution of d4T for AZT in the setting of anaemia or NVP for EFV when there is CNS toxicity).

For some life-threatening toxicities, it may not be possible to identify an optimal substitute drug. For example, with NVP-associated Stevens – Johnson syndrome, most clinicians would avoid substituting another NNRTI drug (EFV) because of the potential for class-specific toxicity. This would require a change to either a triple NRTI regimen (i.e. substituting ABC, for NVP), or substituting a PI for NVP, thereby introducing a drug class usually reserved for second-line regimens.

Table 13: Severe toxicities of ARVs in infants and children, and potential drug substitutions

Toxicity event	Responsible ARV	Suggested first - line ARV drug substitution
Acute symptomatic hepatitis [a] Hypersensitivity reaction Severe or life-threatening rash (Stevens – Johnson syndrome) [c]	NVP	EFV [b] Preferred substitution of NVP to: • a third NRTI (disadvantage: may be less potent) or •PI (disadvantage: premature start of class usually reserved for second-line) [d]
Lactic acidosis Peripheral neuropathy Pancreatitis Lipoatrophy/metabolic syndrome [g]	d4T	ABC [e] AZT or ABC [f] ABC
Severe anaemia [h] or neutropaenia [i] Lactic acidosis Severe gastrointestinal intolerance [j]	AZT	d4T or ABC ABC [e] d4T or ABC
Persistent and severe central nervous system toxicity [k] Potential teratogenicity (adolescent girls in first trimester of pregnancy, or of childbearing potential and not receiving adequate contraception)	EFV	NVP
Hypersensitivity reaction	ABC	AZT
Lipoatrophy/metabolic syndrome Dyslipidaemia Severe diarrhoea	LPV/r [l]	NNRTI

Note: 3TC/FTC-associated pancreatitis has been described in adults but is considered very rare in children.

(a) Symptomatic NVP-associated hepatotoxicity is very rare in HIV-infected children before adolescence.

(b) EFV is not currently recommended for children <3 years of age, and should not be given to postpubertal adolescent girls who are either in the first trimester of pregnancy or are sexually active and not using adequate contraception.

(c) Severe rash is defined as extensive rash with desquamation, angioedema, or a reaction resembling serum sickness; or a rash with constitutional findings such as fever, oral lesions, blistering, facial oedema, conjunctivitis; Stevens – Johnson syndrome can be life-threatening. For life-threatening rash, most clinicians would not substitute EFV because of the potential for NNRTIclass specific toxicity.

(d) The introduction of the PI class of drugs in first-line regimens leads to limitations in the choice of drugs in the event of treatment failure.

(e) Lactic acidosis is least commonly associated with ABC, therefore ABC should replace AZT or d4T whenever lactic acidosis occurs.

(f) In children, ABC or AZT can be considered as an alternative.

(g) Substitution of d4T often may not reverse lipoatrophy.

(h) Exclude malaria in areas where malaria is endemic. Severe anaemia is defined as Hb <7.5 g/dl.

(i) Defined as neutrophil count <500 cells/mm3

(j) Defined as severe, refractory gastrointestinal intolerance that prevents ingestion of ARV drug regimen (e.g. persistent nausea and vomiting)

(k) E.g. persistent hallucinations or psychosis

(l) LPV/r is the only PI recommended as a first-line drug for NVP-exposed infants.

13. Changing therapy for first line treatment failure [2]

Clinical definition of treatment failure

The detection of new or recurrent WHO clinical stage 3 or 4 events in a child on ART may reflect progression of disease, and treatment failure should be considered provided the child is adherent to therapy.

Box 8: Management by using WHO clinical staging of events to guide decision-making on switching to second-line therapy for treatment failure	
New or recurrent clinical event develops after at least 24 weeks on ART [a,b]	**Management options** [c,d]
No new events or stage 1 events	Do not switch to new regimen Maintain regular follow-up
Stage 2 events	Treat and manage event Do not switch to a new regimen Assess adherence and offer support Assess nutritional status and offer support Schedule earlier visit for clinical review and CD4 measurement
Stage 3 events	Treat and manage event and monitor response[e] Check if on treatment 24 weeks or more Assess adherence and offer support Assess nutritional status and offer support Check CD4[f] where available Institute early follow-up
Stage 4 events	Treat and manage event Check if on treatment 24 weeks or more Assess adherence and offer support Assess nutritional status and offer support Check CD4[f] where available Consider switching regimen

(a) A clinical event refers to a new or recurrent condition as classified in the WHO clinical staging at the time of evaluating the infant or child on ART. **(Annexes 1and 3)** provides more details about clinical events.

(b) It needs to be ensured that the child has had at least 24 weeks of treatment and that adherence to therapy has been assessed and considered adequate before considering switching to a second-line regimen.

(c) Differentiating OIs from IRIS is important.

(d) In considering change of treatment because of growth failure, it should be ensured that the child has adequate nutrition and that any intercurrent infections have been treated and have resolved.

(e) Pulmonary or lymph node TB, which are clinical stage 3 conditions, may not be an indication of treatment failure, and thus may not require consideration of second-line therapy. The response to TB therapy should be used to evaluate the need for switching therapy.

(f) CD4 measurement is best performed once the acute phase of the presenting illness has resolved.

Clinical disease progression should be differentiated from IRIS. The worsening of disease after initial clinical improvement or the development of a new or recurrent OI soon after initiating ART in a child does not necessarily indicate treatment failure and is not always an indication to stop or switch ART

Immunological definition of treatment failure

Immunological treatment failure can be identified by assessing the immunological response to ART in relation to baseline CD4.

Providing the child is adherent to the therapy, **immunological failure** is defined as

- A return in CD4 cell percent (or for children >6 years of age, absolute CD4 cell count) to pre-therapy baseline or below, in the absence of other concurrent infection to explain transient CD4 decrease, or
- A >50% fall from peak level on therapy of CD4 cell percent (or for children >6 years of age, absolute CD4 cell count) in the absence of other concurrent infection to explain transient CD4 decrease.
- A rapid CD4 decrease (>30% over six months) or
- Developing or returning to the following age related immunological thresholds after ART for at least 24 weeks

o ≥2 years to < 5 years of age CD 4 count of <200 cells/mm^{3}or % CD4 <10

o ≥5 years of age CD 4 count of <100 cells/mm^3

(Preferably, at least two CD4 measurement should be done)

Virological definition of treatment failure

Where regular access to viral load monitoring is available and affordable, it may be used to identify treatment failure. Viral load is the most sensitive way to detect viral replication. However, individual viral load values do not directly correlate with clinically relevant outcomes (death or disease progression).

Virological failure is recognized if the child is adherent to their (first-line) ART regimen, more than 24 weeks from initiation of ART, and has a persistent viral load over 5 000 copies/ml. In resource-limited settings it may not be feasible to perform viral load testing. The availability of viral load is not a prerequisite for initiation of ART or for the determination of treatment failure.

Box 9: Decision-making on switching to second-line ART for treatment failure based on availability of CD4 measurement		
New or recurrent clinical event on ART	Availability of CD4 measurement	Management options
Stage 1 or stage 2 event	No CD4	Do not switch regimen
	CD4	Consider switching regimen only if two or more values are below the age-related threshold Increase clinical and CD4 follow-up if CD4 value approaches the age-related threshold Measure VL if available
Stage 3 event	No CD4	Manage event and assess response
	CD4	- Switching regimen is recommended if CD4 value is below the age-related threshold and particularly if the child initially had a good immune response to ART - Measure VL if available - Increase clinical and CD4 follow-up if CD4 value approaches age-related threshold
Stage 4 event	No CD4	Consider switching regimen
	CD4	Switching regimen is recommended if CD4 value is below the age-related threshold and particularly if the child initially had a good immune response to ART Switching may not be necessary where CD4 value is above age-related threshold VL testing may resolve discordant CD4 results

Decision-making on switching ART using viral load measurement

Children with clinical failure and/or immunological failure may not all have virological failure, and may not need to switch to second-line therapy. However, a delay in switching therapy in a child with high levels of viral replication may lead to greater development of resistance and compromise the virological activity of standard second-line regimens. It is unclear whether this translates to compromised clinical outcomes. Therefore, in the context of accurately identifying treatment failure, measurement of viral load is useful. Viral load is recommended where available to confirm clinical and/or immunological failure.

Second-line regimen in the event of treament failure

Box 10: Choice of second-line regimen in the event of treatment failure
Preferred first- and second-line regimens

Situation	Preferred first-line regimen	Preferred second-line regimen
INFANTS AND CHILDREN <24 MONTHS		
Not exposed to ARV	NVP + 2 NRTIs	LPV/r + 2 NRTIs
Exposed to NNRTI	LPV/r + 2 NRTIs	NNRTI + 2 NRTIs
Unknown ARV exposure	NVP + 2 NRTIs	LPV/r + 2 NRTIs
CHILDREN		
Children 24 months or more	NNRTI + 2 NRTIs	Boosted PI + 2 NRTIs
CONCOMITANT CONDITIONS		
Child or adolescent with severe anaemia	NVP + 2 NRTIs no AZT	Boosted PI + 2 NRTIs
Child or adolescent with TB	EFV + 2 NRTIs or 3 NRTIs	Boosted PI + 2 NRTIs
Adolescent with hepatitis B	TDF + 3TC + NNRTI	Boosted PI + 2 NRTIs

Box 11:Recommended second-line regimens in infants and children in the event of treatment failure of first-line regimens

Recommended second-line regimen : boosted PI component + two NRTI components

Preferred second-line regimen

First-line regimen at failure	RTI components (NRTI/NNRTI) [a]		PI component	Strength of recommendation	Quality of evidence
2 NRTIs + 1 NNRTI: AZT- or d4T-containing	ABC + 3TC or ABC + ddI	plus	LPV/r[d]	Strong	Moderate
or ABC-containing	AZT + 3TC or AZT + ddI		LPV/r[d]	Strong	High
Triple NRTI	ddI [d] + EFVc or NVP				

(a) Continuation of 3TC in second-line regimens may be considered.

(b) ddI may not need to be taken on an empty stomach in children.

(c) EFV is currently not recommended for children <3 years of age, and should be avoided in post pubertal adolescent girls who are either in the first trimester of pregnancy or are sexually active and not using adequate contraception.

(d) LPV/r is available as solid and liquid co-formulations.

14. CONSIDERATIONS FOR INFANTS AND CHILDREN WITH TUBERCULOSIS AND HIV

Isoniazid Preventive Therapy (IPT) [2, 18]

HIV infected children have the highest risk of developing progression to disease once infected with Mycobacterium tuberculosis, the younger children being at the highest risk.

Systematic review on impact of tuberculosis preventive therapy on tuberculosis and mortality in HIV infected children showed that the outcome of HIV infected children with TB co infection was poor with increased mortality by six fold and cure rate of TB in those children was significantly lower than that of HIV uninfected children and there was a higher rate of recurrence (Gray et al, 2009). Therefore prevention has become an important strategy to reduce mortality and morbidity of TB in HIV/AIDS. Isoniazid is cheap and bactericidal against both extracellular and intracellular bacilli. In latent TB infection the bacterial burden is small allowing the possibility of monotherapy. Therefore to prevent the co infection of TB infection in HIV infected children one needs to get Isoniazid Preventive Therapy (IPT). It is even more important to exclude active TB disease in TB/HIV co infected patients which might not be so easy. Patient must be referred to the next level of care to exclude active TB disease before deciding to administrate IPT.

To provide IPT to children, without active TB, who have contact with TB patients (regardless of HIV co-infection) is a policy of NTP, approved by MOH. (Ref. National guidelines on management of TB in children, NTP, 2007)

TB contact tracing should also be carried out in all the HIV infected children of all ages.

The recommended dose of Isonized (INH) for preventive therapy in HIV co infection is10 mg/kg daily for 6 months (maximum 300 mg/day).

It is necessary to maintain a high index of suspicion of TB whenever the clinical presentation is compatible, regardless of whether IPT has been given.

Treatment of TB in HIV-infected infants and children [2]

The underlying principles for the treatment of TB in HIV-infected children are the same as for children who are not HIV-infected. However, the co-management of TB and HIV, and the treatment of HIV infection, is complicated by drug interactions, particularly between rifampicin and the NNRTI and PI classes of ARVs. These drugs have similar routes of metabolism and co-administration may result in sub-therapeutic drug levels. ART should not be interrupted but dose adjustments of ART may be needed when taken with the rifamycins, especially rifampicin. The potential use of rifabutin, considered in adults to overcome drug – drug interactions, is not recommended due to insufficient data and lack of an available formulation in children. In addition, the choice of ART regimen in TB/HIV co infected children is complicated by the relatively limited number of available pediatric ARV formulations and the lack of dosing information for some ARVs (particularly for children less than 3 years of age).

Any child with active TB disease should begin TB treatment immediately, and start ART as soon as tolerated(2 to 8 weeks of TB therapy) irrespective of the CD4 count and clinical stage.

The preferred first-line ARV regimen for infants and children less than 2 years of age who have been exposed to NVP and are taking a rifampicin-containing regimen for TB is a triple NRTI regimen.

For all HIV-infected infants and children, who develop TB on ART anti-TB therapy should be started immediately upon the diagnosis of TB; ART should continue.

Choice of first-line ARV regimens in children receiving rifampicin-containing TB treatment

Box 12 : Preferred ARV regimens for TB/HIV coinfected infants and children <3 years of age
2 NRTIs + NVP* (except for infants and children <2 years if previously exposed to NVP) OR 3 NRTIs: (d4T or AZT) + 3TC + ABC

Since rifampicin is known to reduce levels of NVP, do not use lead-in dosing of NVP when initiating NVP-containing ART with TB treatment.

Rifampicin lowers the drug level of Nevirapine by 20 to 58% and that of EFV by 25%. In children, there is no information on the appropriate dosage for NVP and EFV when used with Rifampicin. Standard dosage of EFV can be used.

Box 13 : Preferred ARV regimens for TB/HIV coinfected children >3 years of age
2 NRTIs + EFV OR 3 NRTIs: (d4T or AZT) + 3TC + ABC

After completion of Rifampicin based treatment, consider switching treatment to standard 1st line regimen 2NRTI+NVP or EFV.

IRIS in the context of co-therapy for TB/HIV

IRIS has been observed in children receiving anti-TB therapy who have initiated ART. This syndrome is primarily reported in adults, but is also seen in children. A clinical case definition of paradoxical TB-associated IRIS (table 14) will be used for diagnosis. Where available, an increase in CD4 count and a decrease in viral load since start of ART would further support the diagnosis of IRIS. Some cases of IRIS in HIV-infected children may in fact be TB. Other cases may be localized or disseminated BCG disease in children who have received a BCG vaccination. HIV-infected children suspected of having disseminated BCG disease should be referred to an appropriate expert for management, as the diagnosis of BCG disease is difficult and the treatment is specialized.

Table 14 : Clinical case definition of paradoxical TB-associated IRIS

Antecedent requirements	Both of the following requirements must be met: 1. Diagnosis of TB in line with WHO recommendations is made before starting ART 2. A good initial response to TB therapy is observed before the patient started on ART
Clinical criteria	The onset of TB-associated IRIS should be within 3 months of starting ART with at least one major criterion and two minor criteria: Major criteria: • New/enlarging lymph nodes or other focal tissue enlargement • New/worsening radiological features • New/worsening CNS tuberculosis • New/worsening serositis Minor criteria: • New/worsening constitutional symptoms such as fever • New/worsening respiratory symptoms such as cough • New/worsening abdominal pain
Alternative explanations for clinical deterioration excluded	• Poor adherence to TB therapy • Failure of TB therapy due to TB drug resistance • Another OI or neoplasm • Drug toxicity or drug reaction

Table 15 : Recommendations for the timing of ART following the initiation of TB treatment with a rifampicin-containing regimen in HIV-infected infants and children

Clinical stage of child with TB(as an event indicating need for ART)	Timing of ART following initiation of TB treatment (rifampicin-containing regimen)[a]	Recommended ART regimen[b]
Any CD4 count and any WHO clinical stage of HIV for infants and children	Start ART soon after TB treatment between 2 and 8 weeks following start of TB treatment.	**In children <3 years** Preferred first-line regimen Two NRTIs + NVP[b] (Except if <2 years of age and previously exposed to NVP) or Triple NRTI first-line regimen (d4T or AZT) + 3TC + ABC **In children ≥3 years:** Preferred first-line regimen Two NRTIs + EFV[c] or Triple NRTI first-line regimen (d4T or AZT + 3TC + ABC) In chidren who have been started on a triple NRTI regimen for the purposes of TB/HIV co-treatment, it is preferable to switch to a standard first line regimen on completion of TB treatment

(a) Administration of co-trimoxazole prophylaxis is important in children with TB/HIV co infection.

(b) Lead-in dosing should not be used when initiating NVP-containing ART with TB treatment. In addition, the NVP dose should be close to the maximum target dose of 200 mg/m^2. Careful clinical monitoring with laboratory support, if available, is recommended where NVP is administered concurrently with rifampicin.

(c) EFV is not currently recommended for children <3 years of age, and should not be given to postpubertal adolescent girls who are either in the first trimester of pregnancy or are sexually active and not using adequate contraception.

Table 16 : Recommendations for co-management of TB and HIV in infants and children diagnosed with TB while on ART

Time of TB diagnosis in relation to ART	Underlying cause of TB	Considerations for ART following initiation of TB treatment (rifampicin-containing regimen)[a]	ART regimen
Child on first-line regimen with 2 NRTIs + NNRTI diagnosed with TB	TB attributable to primary infection (consider at any time during ART, depending on exposure to TB)	Continue ART but assess for need to change ART regimen – response to TB therapy should be used to evaluate need for change	Continue on standard two NRTIs + NNRTI first-line; if on NVP [b], substitute with EFV [c] if the child is≥3 years; if <3 years increase NVP to maximum dose or Substitute NNRTI to triple NRTI first-line regimen
	TB as part of IRIS (consider in first 6 months of ART)		
	TB as a sign of treatment failure of first-line regimen (consider only after at least 24 weeks of ART)		Consider consultation with experts for construction of second-line regimen [d]
Child on standard PI regimen (2 NRTIs + boosted PI) diagnosed with TB	TB attributable to primary infection (consider at any time during ART, depending on exposure toTB)	Assess for need to change regimen – response to TB therapy should be used to evaluate need for changing or stopping	Continue same regimen,consider adding RTV to achieve full therapeutic dose (increase RTV until same dose as LPV in mg, in a ratio of 1:1) Consider consultation with experts for construction of salvage regimen [d]
	TB as a sign of treatment failure of second-line regimen		Consider consultation with experts for construction of salvage regimen [d]

(a) Administration of co-trimoxazole prophylaxis is important in children with TB/HIV coinfection.
(b) Careful clinical and laboratory monitoring should be ensured where NVP is administered concurrently with rifampicin.
(c) EFV is not currently recommended for children <3 years of age, and should not be given to post pubertal adolescent girls who are either in the first trimester of pregnancy or are sexually active and not using adequate contraception.
(d) Few data are available to guide ART recommendations; research is urgently needed.

15. HIV and Nutrition

1. HIV-infected children should be routinely assessed for nutritional status, including weight and height at scheduled visits, particularly after initiation of ART.
2. HIV-infected children on or off ART who are symptomatic, have conditions requiring increased energy (e.g. TB, chronic lung disease, chronic OIs or malignancies), or have weight loss or evidence of poor growth should be provided with 25 – 30% additional energy.
3. HIV-infected children who are severely malnourished should be managed as per the guidelines for uninfected children and provided with 50 – 100% additional energy.
4. HIV-infected children should receive one recommended daily allowance (RDA) of micronutrients daily. If this cannot be assured through the diet, or there is evidence of deficiency, then supplementation should be given.
5. HIV-infected infants and children between 6 and 59 months of age should receive high-dose vitamin .A supplementation every 6 months, as per the guidelines for uninfected children.
6. HIV-infected children who have diarrhoea should receive zinc supplementation as part of management, as per the guidelines for uninfected children.
7. For infants and young children known to be HIV infected, mothers are strongly encouraged to exclusively breastfeed for 6 months and continue breastfeeding as per recommendations for the general population (up to two years of age and beyond).

Effects of HIV on Nutrition

Increased food needs	To fight infection Immune system works harder Increased energy and nutrient requirements Further infection and fever Increased body demand for food Needs more food if symptoms develop
Reduced food intake	Illness and medicine taken Reduced appetite Sore mouth, nausea and vomiting Tiredness, isolation and depression Reduced appetite and willingness to make an effort to prepare food and eat regularly Economic issue Lack of awareness if importance of nutrition
Reduced absorption of food	Damaged intestinal wall Diarrhoea Weight loss and malnutrition
Altered body function	Diabetes Excess and breakdown of body muscles Edema Fat intolerance

Effect of Nutrition on HIV

- Well nourished HIV-infected person
- Improved quality of life
- Active
- Ability to care for themselves
- Reduced illness from infections and recover more quickly
- Good appetite and stable weight
- Good earning capacity and able to help the family and reduced the cost of health care
- No school absenteeism, better education and development
- More energy

HIV and infant feeding [2]

- 4-12% risk of transmission by breast milk after 6 months of delivery
- Risk increased to 20% if breastfed for at least 24 months

Mother known to be HIV infected should follow the following recommendations.

1. Mothers known to be HIV-infected should be provided with lifelong ART or ARV prophylaxis interventions to reduce HIV transmission through breastfeeding according to WHO recommendations.
2. Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

3. When mothers decide to stop breastfeeding

   Mothers known to be HIV-infected who decide to stop breastfeeding at any time should stop gradually within one month. Mothers or infants who have been receiving ARV prophylaxis should continue prophylaxis for one week after breastfeeding is fully stopped.

   Stopping breastfeeding abruptly is not advisable.

4. What to feed infants when mothers stop breastfeeding

   When mothers known to be HIV-infected decide to stop breastfeeding at any time, infants should be provided with safe and adequate replacement feeds to enable normal growth and development.

Alternatives to breastfeeding include:

For infants less than six months of age:

- Commercial infant formula milk as long as home conditions outlined in Recommendation #5 are fulfilled;
- Expressed, heat-treated breast milk
- Home-modified animal milk is not recommended as a replacement food in the first six months of life.

For children over six months of age:

- Commercial infant formula milk as long as home conditions outlined in Recommendation #5 are fulfilled;
- Animal milk (boiled for infants under 12 months), as part of a diet providing adequate micronutrient intake;
- Meals, including milk-only feeds, other foods and combination of milk feeds and other foods, should be provided four or five times per day.1 All children need complementary foods from six months of age.

5. Conditions needed to safely formula feed

Mothers known to be HIV-infected should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status, when specific conditions are met:
(referred to as AFASS – affordable, feasible, acceptable, sustainable and safe- in 2006 WHO recommendation on HIV and infant feeding)

a. safe water and sanitation are assured at the household level and in the community; and
b. the mother, or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant; and
c. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition; and
d. the mother or caregiver can, in the first six months, exclusively give infant formula milk; and
e. the family is supportive of this practice; and
f. the mother or caregiver can access health care that offers comprehensive child health services.

- Education on safe preparation should be mentioned clearly for healthcare providers such as how to wash hands before milk preparation, how to prepare formula safely and appropriately step by step, how to give written instructions on safe preparation of formula eg. take home flyers mentioning the risks of replacement feeding and how to avoid them, advise when to seek care and about the follow-up visit.

6. Heat-treated, expressed breast milk
Mothers known to be HIV-infected may consider expressing and heat-treating breast milk as *an interim feeding strategy*:

- in special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; **or**
- when the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis; **or**
- to assist mothers to stop breastfeeding; **or**
- if antiretroviral drugs are temporarily not available.

7. When the infant is HIV-infected
If infants and young children are known to be HIV-infected, mothers are strongly encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding as per the recommendations for the general population, that is, up to two years or beyond.

Strategies to reduce breast milk transmission

1. Birth to 6 months of age

Replacement Therapy	Feeding an infant who is receiving no breast milk with a diet that provides all the nutrients the infant needs until the age at which he/she can be fully fed on family foods
A Acceptable	• No barriers to replacement feeding • Cultural, social reasons • Fear of stigmata or discrimination
F Feasible	• Adequate time, knowledge, skills • frequent feeding
A Affordable	• Cost of ingredients, fuel, soap, water and equipment
S Sustainable	• Continuous and uninterrupted procedure
S Safe	• Correctly and hygienically prepared and stored • Adequate amount
	• Early cessation of breastfeeding • No specific time is recommended • Until the time they can provide replacement therapy
Modified Breastfeeding	• Expressed and heat-treated breast milk • Pasteurized expressed breast milk (heat to 62.5 C for 30 min) or boiled and cooled immediately • Time consuming and needs refrigerator, clean container • Not practical for long-term • Useful for sick or low birth weight babies in hospital

Breast milk substitutes	**Commercial Infant Formula** • Closest in nutrient composition to breast milk • No anti-infective properties • Over concentration and Overload with salt and amino acids • Over-dilution may occur • Very expensive • Can be considered if family has reliable access to formula • Give extra water **Home prepared formula** • Animal milks • Composition not the same, e.g., deficient in micronutrients • Danger of over concentration or over dilution **Dried milk powder and evaporated milk** • Can be modified • Micronutrient supplementation required **Unmodified cow's milk** • Not recommended • If used, must give extra water **Breast milk banks** • Source of breast milk for a short time e.g., for sick and LBW babies • Risk of HIV transmission • Need screening **Wet-Nursing** • Relative breastfeeding on infant • HIV testing • Informed of her risk • counseling

2. 6 months to 2 years

Table : 17 Introducing complementary feeding

Age months	Texture	Frequency	Amount each meal
6	Soft, porridge well meshed foods	2 per day	2-3 tsp
7-8	Mashed food	3 per day	2/3 cup
9-11	Finely chopped or mashed foods and foods that baby can pick up	3 meals plus 1 snack between meals	¾ cup
12-24	Family foods, chopped or mashed	3 meals plus 2 snacks in between meals	1 full cup

Feeding the child who is ill

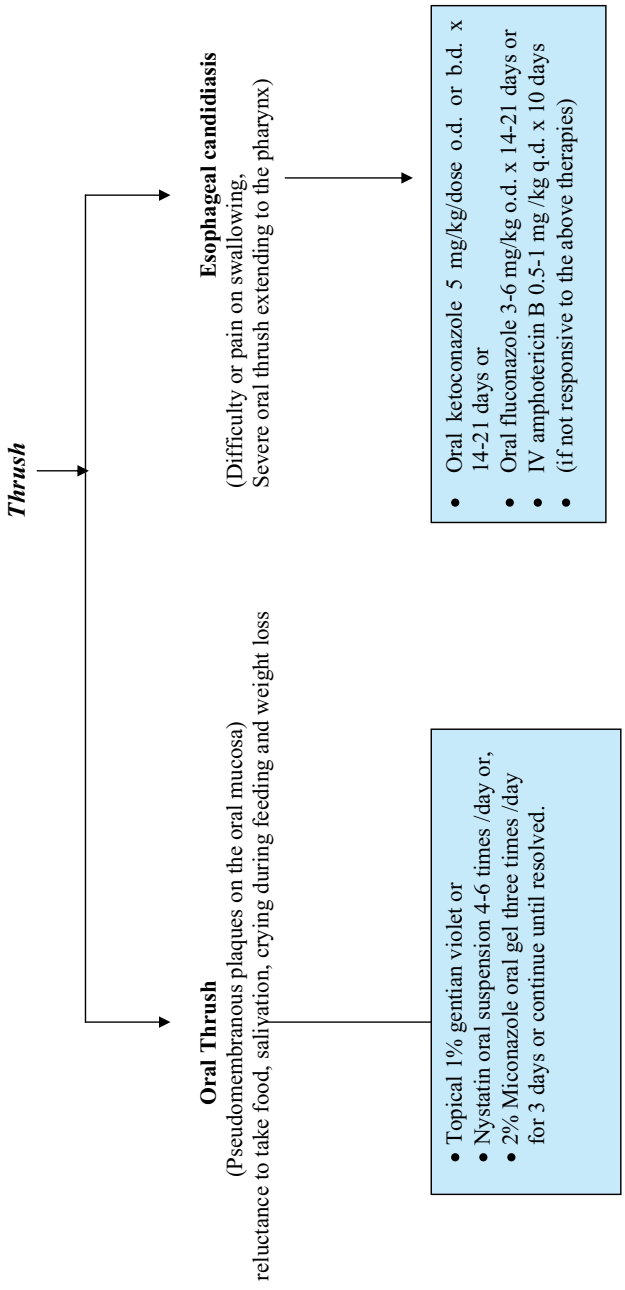
- Make the child comfortable
- Be patient and feed slowly
- Feed small amounts frequently
- Give foods that the child likes

Give a variety of foods and extra fluid

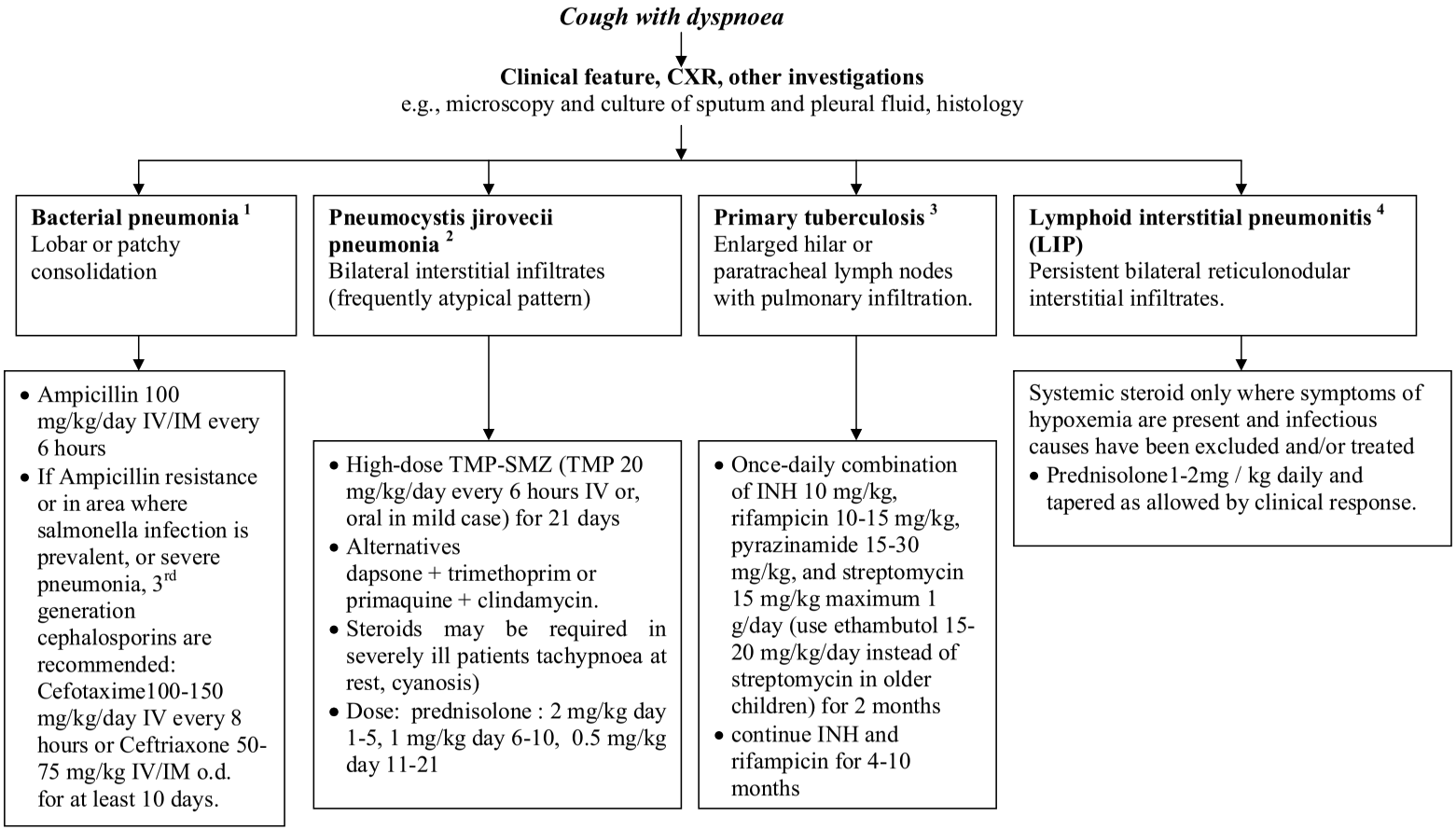
Principles of Complementary feeding
Milk & complementary 3 times/day
If no more milk → feed 5 times/day
Hygienic preparation Gradual introduction
Quantities needed to increase
One item after another
Gradually concentrated
Correct mixing
Feeding method

18. Diagnosis and treatment of opportunistic infections in HIV-infected children

Thrush (candidiasis)



Respiratory infections



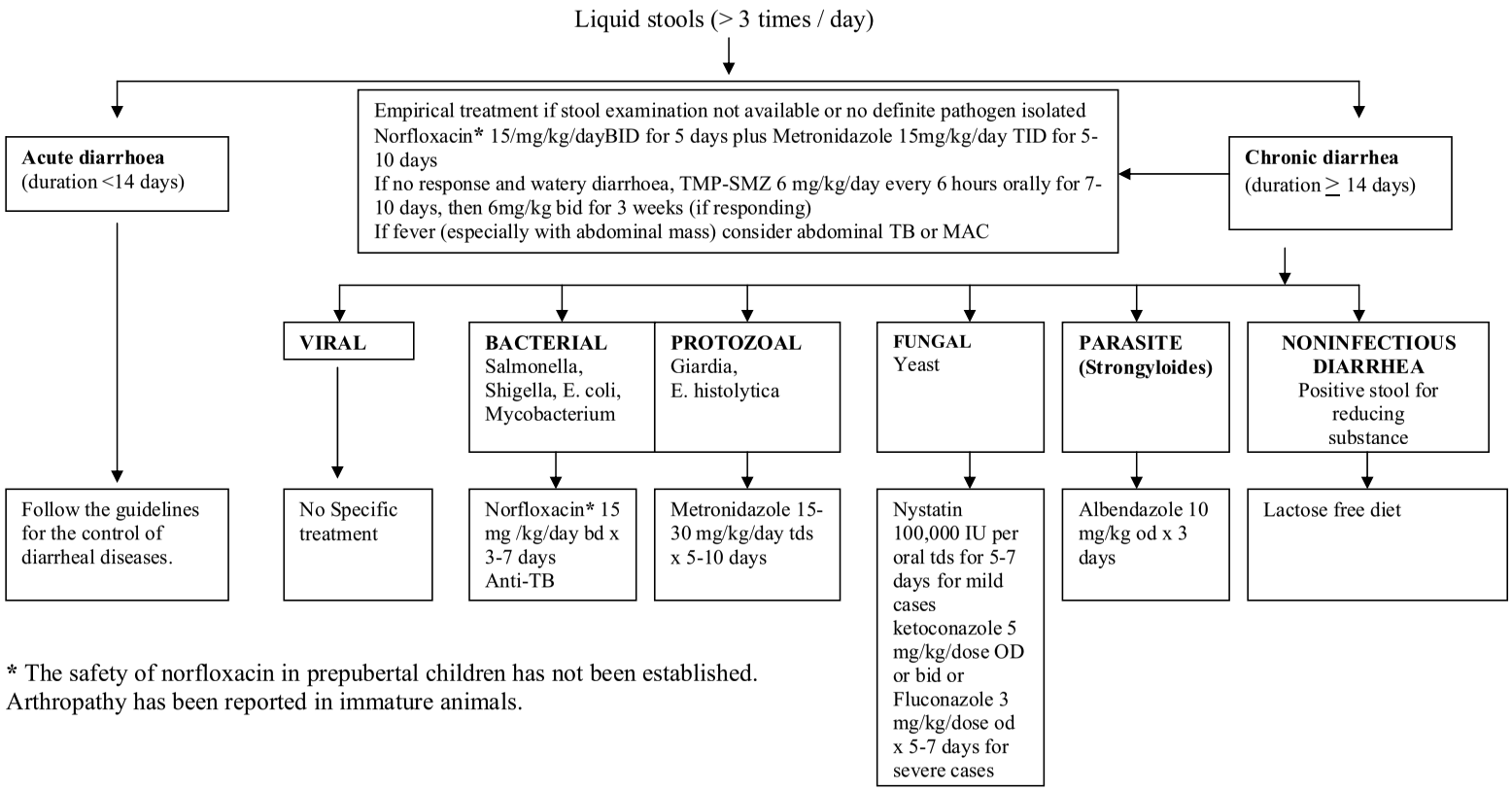
NOTES ON RESPIRATORY INFECTIONS

Several pathogens can be present at the same time.
CXR is often is often non-specific and interpretation can be difficult. Clinical assessment is also required.

	1. Bacterial pneumonia	2. Pneumocystis jirovecii pneumonia	3. Primary tuberculosis	4. Lymphoid interstitial pneumonitis
Chest Ray	Lobar or patchy consolidation	Bilateral interstitial infiltrates (frequently atypical pattern)	Enlarged hilar or paratracheal lymph nodes with pulmonary infiltration.	Persistent bilateral reticulonodular interstitial infiltrates.
Clinical signs	Acute onset, productive cough, abnormal chest auscultation, toxic signs	Acute or sub acute onset of symptoms, prominent dyspnoea and tachypnoea, wheezes and rhonchi, progressive fever, dry cough, usually normal chest auscultation Organism- Silver stain from BAL, biopsy, gastric fluid aspirate	Gradual onset, prominent wasting and fever, usually normal chest auscultation, family contact with TB may be present.	Gradual chronic progressive onset, afebrile, cough, wheezing, dyspnoea, signs of chronic respiratory insufficiency. Auscutatory findings are rare in early stage, lymphadenopathy, clubbing, Consider in children with no response to antibiotics and to empirical anti-TB therapy

Note on LIP
LIP is a chronic lung disorder of unknown cause that affects up to 40% to 50% of perinatally acquired HIV-infected children. Chest X-ray shows a bilateral diffuse, interstitial, reticulonodular infiltrates. Clinically, there is a wide spectrum of severity, from asymptomatic to and oxygen dependency. LIP may also remit spontaneously. A presumptive diagnosis may be made on the basis of suggestive x-ray changes that persist for months, are unresponsive to antimicrobial therapy, and are not the result of other specific infectious pathogens. PCP can co-exist with LIP.

Diarrhoea

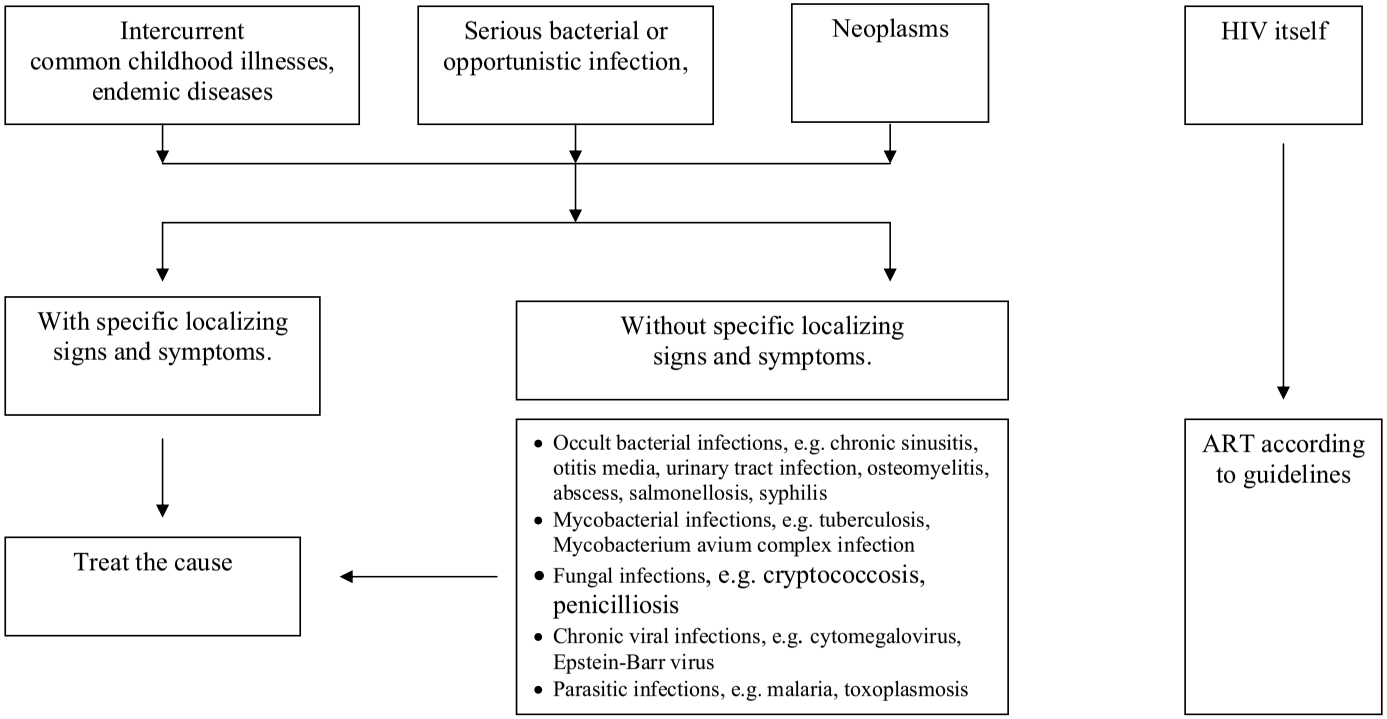


* The safety of norfloxacin in prepubertal children has not been established. Arthropathy has been reported in immature animals.

Persistent or recurrent fever

(Fever is defined as body temperature of 37.5º C axilla, 38.0º C oral, 38.5º C rectal.)

- Persistent fever: Fever for more than 5 days duration.
- Recurrent fever: Fever for more than one episode over a period of 5 days.



Neurological abnormalities

Progressive encephalopathy: Progressive decline in motor, cognitive, or language function, evidence of loss or increasing delay in developmental milestone achievement;

Static encephalopathy: Motor dysfunction and other developmental deficits of varying severity that are non-progressive

Acute episodes: Acute onset of seizures, focal neurological abnormalities (e.g. toxoplasmosis[1]) or meningism (e.g. cryptococcal meningitis[2], bacterial meningitis, tuberculous meningitis[3] or cytomegalovirus encephalitis

Acute deterioration can also be secondary to drug treatment side effects, such as peripheral neuropathy from ddI

A careful history and physical examination including neurological examination and development examination
Lumbar puncture if meningitis suspected

- ART regimens including either AZT or d4T due to high CNS penetration
- For empirical treatment prior to identification of pathogen.
- - Cefotaxime 200-300 mg/kg/day every 6-8 hours, is recommended.

- Empirical treatment in the neonate (up to 28 days) is ampicillin 200-300 mg/kg/day IV every 6 hours, plus gentamicin 7.5 mg/kg/day IV every 8 hours .or cefotaxime 200 mg/kg/day IV every 6 hours plus gentamicin 7.5 mg/kg/day IV every 8 hours.

- If a pathogen is identified[4], treat accordingly.

Notes for neurological abnormalities

1. Toxoplasma encephalitis
   - Fever, focal neurological deficit (2 ring enhancing lesions on MRI)
   - Positive anti-Toxoplasmosis gondii lgG

   Focal neurological signs: start presumptive treatment for toxoplasmosis (improvement should be seen within 7-10 days if diagnosis is correct). Toxoplasmosis treatment: Pyramethamine loading does 2mg/Kg/day BID for two days, then 1mg/kg once daily for 6 weeks plus Sulphadiazine 120mg/kg/day QID for 6 weeks plus folinic acid 5mg (if available) every 2-3 days.
   If signs of raised intracranial pressure are present: add prednisolone 2 mg/kg qid; after 5 days (or when signs of improvement), taper dose with 0.5 mg/kg every 5 days.

2. Cryptococcal Meningitis
   - Fever, headache, meningism, usually sub acute
   - Vesicular or papular skin lesions my be present
   - Pneumonitis may be present
   - Positive CSF, stain (positive serum cryptococcal Ag)

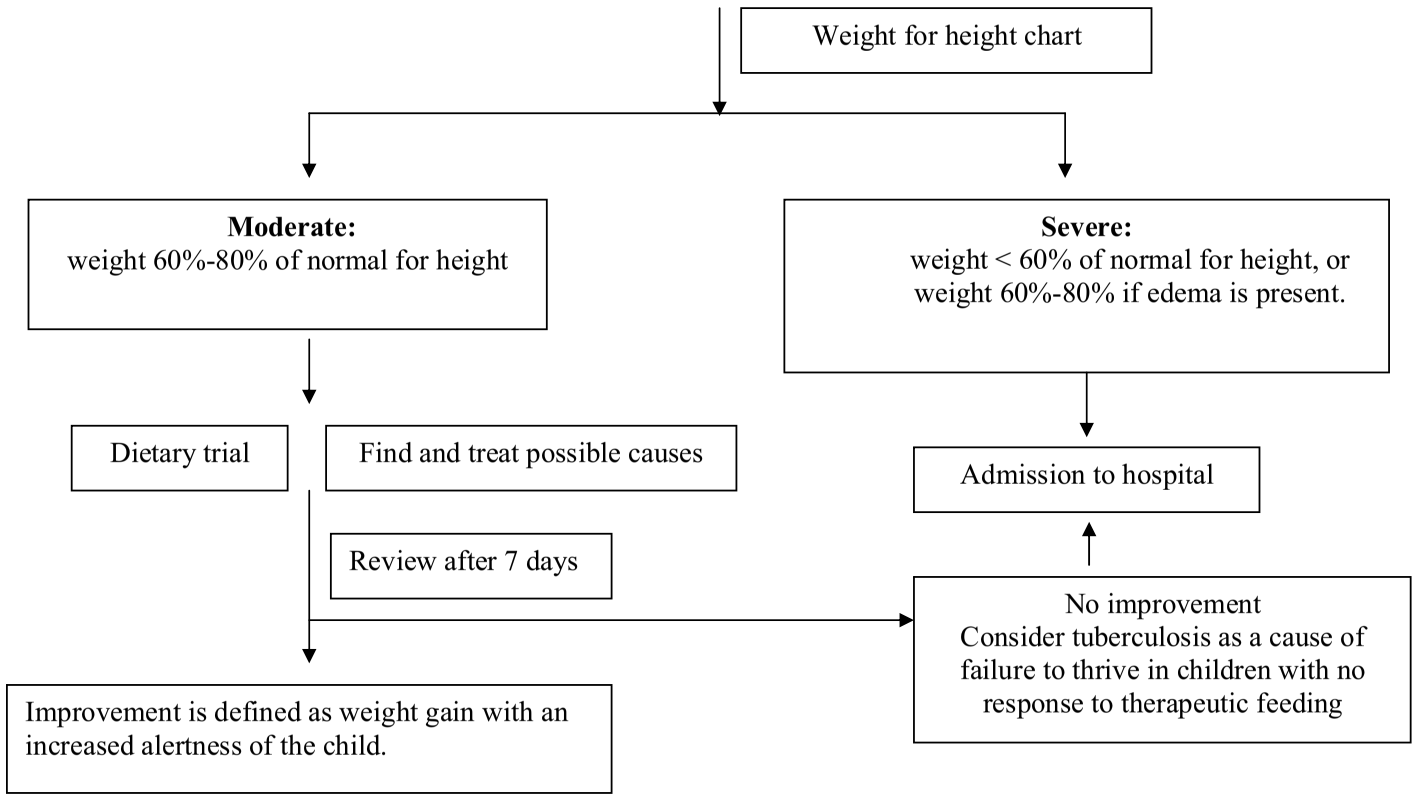
   For patients without neurological signs, lumbar puncture should be performed.
   Cryptococcal meningitis treatment: Amphotericin B 0.5-1mg/kg/day IV infusion once daily over 4-6 hours for 2 weeks, followed by fluconazole 12mg/kg/day every 12-24 hours for 8 weeks.

3. Treatment of tuberculous meningitis (Follow National tuberculosis treatment guidelines)

4. CMV encephalitis
   - Rapidly progressing delirium, cranial nerve defects, ataxia, nystagmus
   - CSF-protein, mononuclear pleocytosis
   - MRI- Periventricular enhancement
   - CMV by PCR in CSF or brain

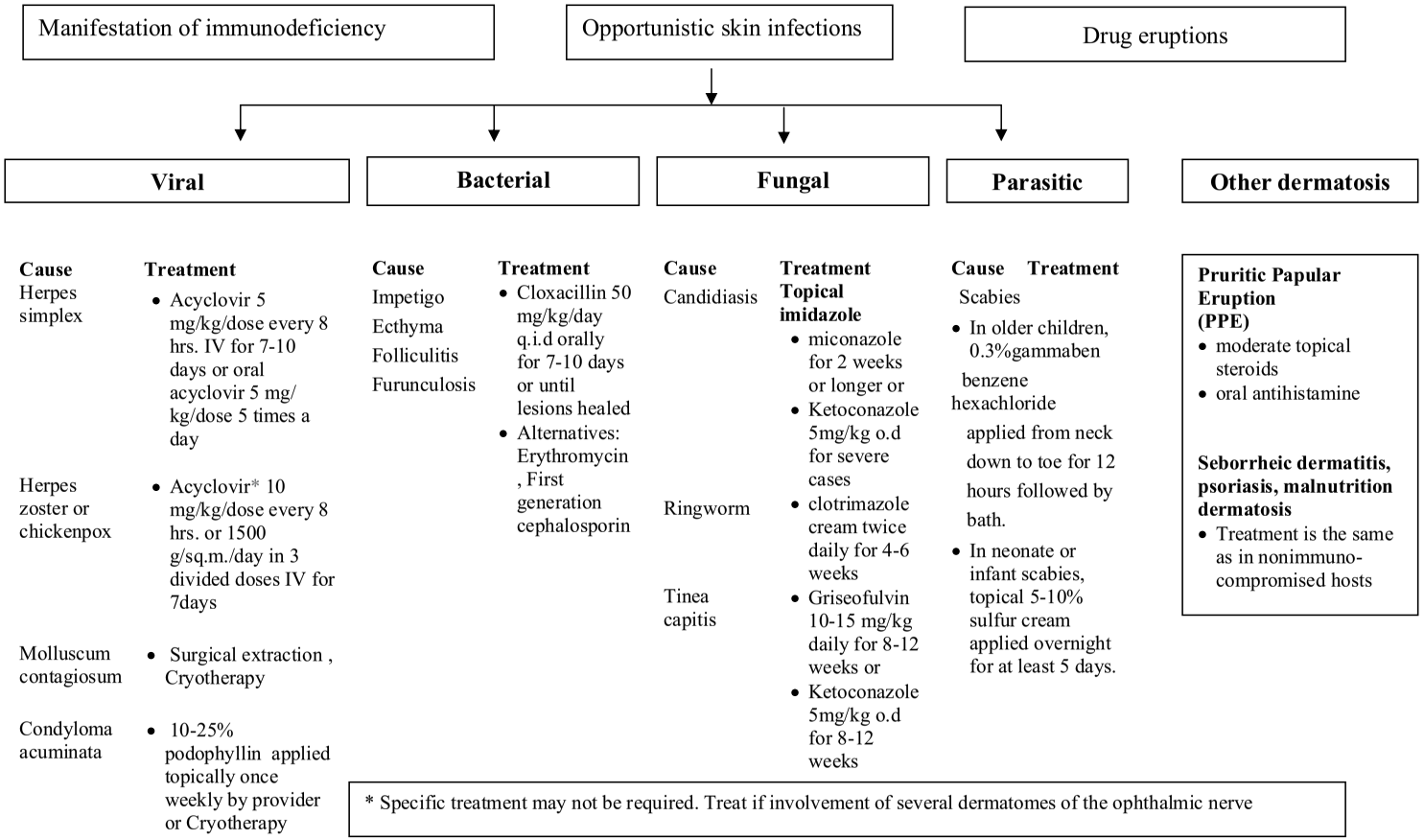
Failure to thrive

(Failure to thrive should be suspected if a child deviates from own apparent path of growth.)



HIV-associated skin diseases in children

(The presence of dermatitis in children with HIV infection)



Annex 1

WHO Clinical Staging of HIV for Infants and Children with Established HIV Infection

Clinical stage 1
Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2
Unexplained persistent hepatosplenomegaly Papular pruritic eruptions 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
Unexplained moderate malnutrition not adequately responding to standard therapy Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (above 37.5 oC, intermittent or constant, for longer than one month) Persistent oral Candidiasis (after first 6 weeks of life) Oral hairy leukoplakia Acute necrotizing ulcerative gingivitis/periodontitis Lymph node TB Pulmonary TB Severe recurrent bacterial pneumonia Symptomatic lymphoid interstitial pneumonitis Chronic HIV-associated lung disease including bronchiectasis Unexplained anaemia (<8.0 g/dl), neutropenia (<0.5x10^9/L3) or chronic thrombocytopenia (<50 x 10^9/L3)

Clinical stage 4

Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
Pneumocystis pneumonia
Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration, or visceral at any site)
Extrapulmonary TB
Kaposi sarcoma
Oesophageal candidiasis (or candiadisis of trachea, bronchi or lungs)
Central nervous system toxoplasmosis (after the neonatal period)
HIV encephalopathy
Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age more than 1 month
Extrapulmonary cryptococcosis including meningitis
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)
Chronic cryptosporidiosis (with diarrhoea)
Chronic isosporiasis
Disseminated non-tuberculous mycobacterial infection
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
HIV-associated cardiomyopathy or nephropathy

Annex 2

Weight for length table

Young children, sexes combined, 52-108 cm in length

LENGTH (cm)	WEIGHT (kg)				
	Standard	90% Standard	80% Standard	70% Standard	60% Standard
52	3.8	3.4	3.0	2.7	2.3
53	4.0	3.6	3.2	2.8	2.4
54	4.3	3.9	3.4	3.0	2.6
55	4.6	4.1	3.6	3.2	2.7
56	4.8	4.3	3.8	3.4	2.9
57	5.0	4.5	3.9	3.5	3.0
58	5.2	4.7	4.2	3.6	3.1
59	5.5	4.9	4.4	3.8	3.3
60	5.7	5.1	4.6	4.0	3.4
61	6.0	5.4	4.8	4.2	3.6
62	6.3	5.7	5.0	4.4	3.8
63	6.6	5.9	5.3	4.6	3.9
64	6.9	6.2	5.5	4.8	4.1
65	7.2	6.5	5.8	5.0	4.3
66	7.5	6.8	6.0	5.3	4.5
67	7.8	7.0	6.2	5.5	4.7
68	8.1	7.3	6.5	5.7	4.9
69	8.4	7.6	6.7	5.9	5.0
70	8.7	7.8	7.0	6.1	5.2
71	9.0	8.1	7.2	6.2	5.3
72	9.2	8.3	7.4	6.4	5.5
73	9.5	8.5	7.6	6.6	5.6
74	9.7	8.7	7.8	6.8	5.8
75	9.9	9.0	8.0	6.9	5.9
76	10.2	9.2	8.1	7.1	6.1
77	10.4	9.4	8.3	7.2	6.3
78	10.6	9.5	8.5	7.4	6.4
79	10.8	9.7	8.6	7.5	6.5
80	11.0	9.9	8.8	7.7	6.6
81	11.2	10.1	9.0	7.8	6.7
82	11.4	10.3	9.1	8.0	6.8
83	11.6	10.4	9.2	8.1	6.9
84	11.8	10.6	9.4	8.3	7.1
85	12.0	10.7	9.6	8.4	7.2
86	12.2	11.0	9.8	9.5	7.3
87	12.4	11.1	9.9	8.6	7.4
88	12.6	11.3	10.1	8.8	7.6
89	12.8	11.5	10.3	9.0	7.7
90	13.1	11.8	11.5	9.2	7.9
91	13.4	11.9	11.8	9.3	8.0
92	13.6	12.2	11.9	9.5	8.2
93	13.8	12.4	11.0	9.6	8.3
94	14.0	12.6	11.2	9.8	8.4
95	14.3	12.8	11.1	10.0	8.5
96	14.5	13.1	11.6	10.2	8.7
97	14.7	13.3	11.8	10.3	8.8
98	15.0	13.5	12.0	10.5	9.0
99	15.3	13.7	12.3	10.7	9.2
100	15.6	14.0	12.5	10.9	9.4
101	15.8	14.2	12.6	11.1	9.5
102	16.1	14.5	12.9	11.3	9.7
103	16.4	14.7	13.2	11.5	9.8
104	16.7	15.0	13.4	11.7	10.0
105	17.0	15.3	13.6	11.9	10.1
106	17.3	15.6	13.8	12.1	10.4
107	17.6	15.9	14.0	12.3	10.5
108	18.0	16.2	14.4	12.6	10.8

Annex 3

Presumptive and definitive criteria for recognizing HIV-related clinical events

(In infants and children with established HIV infection)

Clincial event	Clinical diagnosis	Definitive diagnosis
Stage 1		
Asymptomatic	No HIV-related symptoms reported and no clinical signs on examination	Not applicable
Persistent generalized lymphadenopathy (PGL)	Persistent swollen or enlarged lymph nodes >1 cm at two or more noncontiguous sites, excluding inguinal, without known cause	Clinical diagnosis
Stage 2		
Unexplained persistent hepatosplenomegaly	Enlarged liver and spleen without obvious cause	Clinical diagnosis
Papular pruritic eruptions	Papular pruritic vesicular lesions	Clinical diagnosis
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.	Clinical diagnosis
Angular cheilitis	Splits or cracks on the lips at the angle of the mouth with depigmentation, usually responding to antifungal treatment but may recur	Clinical diagnosis
Lineal gingival erythema (LGE)	Erythematous band that follows the contour of the free gingival line; may be associated with spontaneous bleeding	Clinical diagnosis
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	Clinical diagnosis
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. Giant molluscum may indicate advanced immunodeficiency.	Clinical diagnosis
Recurrent oral ulcerations (two or more in six months)	Aphthous ulceration, typically with a halo of inflammation and yellow-grey pseudomembrane	Clinical diagnosis

Clincial event	Clinical diagnosis	Definitive diagnosis
Stage 2		
Unexplained parotid enlargement	Asymptomatic bilateral swelling that may spontaneously resolve and recur, in absence of other known cause; usually painless	Clinical diagnosis
Herpes zoster	Painful rash with fluid-filled blisters, dermatomal distribution, may be haemorrhagic on erythematous background, and may become large and confluent. Does not cross the midline.	Clinical diagnosis
Recurrent upper respiratory tract infection (URTI)	Current event with at least one episode in past six 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 (laryngotracheal bronchitis [LTB]), persistent or recurrent ear discharge	Clinical diagnosis
Stage 3		
Unexplained moderate malnutrition	Weight loss: low weight-for-age, up to -2 standard deviations (SDs), not explained by poor or inadequate feeding and/or other infections, and not adequately responding to standard management	Documented loss of body weight of -2 SD, failure to gain weight on standard management and no other cause identified during investigation
Unexplained persistent diarrhoea	Unexplained persistent (14 days or more) diarrhoea (loose or watery stool, three or more times daily) not responding to standard treatment	Stools observed and documented as unformed. Culture and microscopy reveal no pathogens.
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.	Documented fever of >37.5 oC with negative blood culture, negative malaria slide and normal or unchanged CXR, and no other obvious foci of disease

Chronic HIV-associated lung disease (including bronchiectasis	History of cough productive with copious amounts of purulent sputum (bronchiectasis only), with or without clubbing, halitosis, and crepitations and/or wheeze on auscultation	CXR: may show honeycomb appearance (small cysts) and/or persistent areas of opacification and/ or widespread lung destruction with fibrosis and loss of volume.
Unexplained anaemia (<8 g/dl), or neutropenia (<0.5 x 109/L) or chronic thrombocytopenia (<50 X 109/L/	No presumptive clinical diagnosis	Laboratory testing, not explained by other non-HIV conditions, or not responding to standard therapy with haematinics, antimalarials or anthelminthics as outlined in the IMCI
Stage 4		
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 in two weeks to 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 the WHO IMCI guidelines	Confirmed by documented weight loss of >-3 SD +/- oedema

Clincial event	Clinical diagnosis	Definitive diagnosis
Stage 4		
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 <6 months of age. Response to high-dose cotrimoxazole +/- prednisolone	Confirmed by: CXR, typical bilateral perihilar diffuse infiltrates; microscopy of induced sputum or BAL or nasopharyngeal aspirate (NPA)
Recurrent severe 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 six months	Confirmed by culture of appropriate clinical specimen
Confirmed by culture of appropriate clinical specimen	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
Oesophageal candidiasis (or candidiasis 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 or macroscopic appearance at bronchoscopy or histology

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	Positive microscopy showing AFB or culture of Mycobacterium tuberculosis from blood or other relevant specimen except sputum or BAL. Biopsy and histology
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	Macroscopic appearance or by histology: • typical red-purple lesions seen on bronchoscopy or endoscopy; • dense masses in lymph nodes, viscera or lungs by palpation or radiology; • histology
CMV retinitis or CMV infection affecting another organ, with onset at age >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 or CMV demonstrated in CSF by culture or DNA-PCR

CNS toxoplasmosis with onset at age >1 month	Fever, headache, focal neurological signs, convulsions. Usually responds within 10 days to specific therapy.	Postive serum Toxoplasma antibody and if available, neuroimaging showing single/multiple intracranial mass lesions
Extrapulmonary cryptococcosis including meningitis	Meningitis: usually subacute, fever with increasing severe headache, meningism, confusion, behavioural changes that respond to cryptococcal therapy	Isolation of Crytococcus neoformans from extrapulmonary site or positive cryptococall antigen test (CRAG) in CSF or blood.

Annex 4

Paediatric drug formulations and doses

Name of drug	Formulations	Pharma-cokinetic data available	Age (weight), dose and dose frequency	Other comments
Nucleoside analogue reverse transcriptase inhibitors				
Zidovudine (ZDV)	Syrup: 10 mg/ml Capsules 100mg ,250 mg Tablet: 60mg 300 mg	All ages	< 4 weeks: 4 mg/kg/dose twice daily 4 weeks to 13 yrs: 180-240 mg/m^2/dose twice daily Maximum dose: ≥13 yrs: 300 mg/dose twice daily	- Large volume of syrup not well tolerated in older children, Syrup needs storage in glass jars and is light sensitive - Can give with food - For children with suspected nervous system involvement, it may be beneficial to use a dose at the higher end of the range. - Capsule can be opened and contents dispersed or tablet crushed and contents mixed with small amount of water or food and immediately taken (solution is stable at room temperature) - Do not use with d4T (antagonistic antiretroviral effect)
Lamivudine (3TC)	Oral solution: 10 mg/ml Tablet: 150 mg	All ages	< 30 days: 2 mg/kg/dose twice daily ≥30 days: 4 mg/kg/dose twice daily Maximum dose: > 50 kg: 150 mg/dose twice daily	- Well tolerated - Can give with food - Store solution at room temperature (use within one month of opening) - Tablet can be crushed and contents mixed with small amount water or food and immediately taken
Fixed-dose combination of ZDV plus 3TC	No liquid available Tablet: 300 mg ZDV Plus 150 mg 3TC 60 mg ZDV Plus 30 mg 3TC	Adolescents and adults	AZT 180-240mg/m2 twice daily 3TC 4mg/kg twice daily	- Ideally, tablet should not be split - Tablet can be crushed and contents mixed with small amount of water or food and immediately taken - At weight <30 kg, ZDV and 3TC cannot be dosed accurately in tablet form

Stavudine (d4T)	Oral solution: 1 mg/ml Capsules: 15 mg, 20 mg, 30 mg,	All ages	< 30 kg: 1 mg/kg/dose twice daily >25kg kg: 30 mg/dose twice daily	- Large volume of solution - Keep solution refrigerated; stable for 30 days; must shake well. Needs to be stored in glass bottles. - Capsules can be opened up and mixed with small amount of food or water (stable in solution for 24 hours if kept refrigerated) - Do not use with ZDV (antagonistic antiretroviral effect)
Fixed combination of d4t plus 3TC	No liquid available Tablet: d4T6mg+3TC30 mg d4T12mg+3TC60mg d4T30mg+3TC150 mg	Adolescents and adults	d4T 1mg/kg twice daily 3TC-4mg/kg t twice daily	Ideally, tablet should not be split See comments under individual drug components
Didanosine (ddI)	Oral suspension paediatric powder/ water: 10 mg/ml. In many countries needs to be made up with additional antacid. Chewable(buffered) tablets: 25 mg; 50 mg; 100 mg;200mg Enteric-coated beadlets in capsules: 125mg; 200 mg;250 mg; 400 mg	All ages	< 3 mon: 50mg/m^2/dose twice daily 3 mon to < 13 yrs: 90-120 mg/m^2/dose twice daily Maximum dose: ≥13 yrs or > 60 kg: 200 mg/dose twice daily or 400 mg once daily	Keeps suspension refrigerated; stable for 30 days; must shake well ddI is degraded rapidly unless given as an enteric formulation (or) combined with buffering agents (or) antacids In children this effect is less marked and ddI may not have to be administered on an empty stomach - If tablets dispersed in water, at least 2 of appropriate strength tablets should be dissolved for adequate buffering - Enteric-coated beadlets in capsules can be opened and sprinkled on small amount of food

Name of drug	Formulations	Pharma-cokinetic data available	Age (weight), dose and dose frequency	Other comments
Abacavir (ABC)	Oral solution: 20 mg/ml Tablet: 60 mg,300mg	Over age 3 months	< 16 years or < 37.5 kg: 8 mg/kg/dose twice daily Maximum dose: > 16 years or ≥37.5 kg: 300 mg/dose twice daily	Can give with food . Tablet can be crushed and contents mixed with small amount water or food andimmediately ingested MUST WARN PARENTS ABOUT HYPERSENSITIVITY REACTION ABC should be stopped permanently if hypersensitivity reaction occurs
Fixed-dose combination of Abacavir (ABC) plus Lamivudine	**Paediatric Tablets** ABC 60 mg + 3TC 30 mg tablets **Adult tablets** ABC 600 mg + 3TC 300 mg	Adolescents and adults	ABC 8mg/kg twice daily 3TC 4mg/kg twice daily	See comments under individual drug components No food restriction
Fixed-dose combination of ZDV plus 3TC plus ABC	No liquid available **Adult Tablet:** ZDV 300 mg + 3TC 150mg + ABC 300 mg **Paediatric Tablet:** ZDV60mg + 3TC 30 mg + ABC60 mg	Adolescents and adults	ZDV180-240mg/m2twice daily 3TC 4mg/kg twice daily ABC 8mg/kg twice daily	See comments under individual drugs components Must warn patient about hypersensitive reaction ABC should be stopped permanently if hypersensitivity reaction occurs

Non-nucleoside reverse transcriptase inhibitors				
Nevirapine (NVP)	Oral suspension: 10 mg/ml Tablet: 200 mg 50mg	All ages	Target dose – maintenance therapy• 160 – 200 mg/m2 to maximum dose of 200 mg twice daily Target dose prophylaxis Aim for exposure of 100ng/ml **• Birth to 6 weeks of age:** - weight less than 2.5 kg 10 mg per day - weight more than 2.5 kg 15 mg per day **• Age 6 weeks to 6 months** 20 mg per day **• Age 6 months to 9 months** 30 mg per day **• Age 9 months to end of breastfeeding** 40 mg per day **Special considerations on maintenance therapy** Induction: during the first 14 days omit the evening dose of NVP. If the morning and evening doses are unequal, give the higher dose in the morning and omit the lower evening dose. **Maintenance therapy:** target dose is 160 – 200 mg/m^2 given twice daily and adjusted for more aggressive dosing in the younger age group.	If rifampicin co-administration, avoid use (see Tuberculosis section) -Store suspension at room temperature; must shake well - Can give with food -Tablets are scored and can be divided into two equal halves to give a 100 mg dose; -can be crushed and combined with small amount of water or food and immediately administered -MUST WARN PARENTS ABOUT RASH -Do not dose escalate if rash occurs (if mild/moderate rash, hold drug; when rash cleared, restart dosing from beginning of dose escalation; if severe rash, discontinue drug) Drug interactions

Name of drug	Formulations	Pharma-cokinetic data available	Age (weight), dose and dose frequency	Other comments
Efavirenz (EFV)	Syrup: 30 mg/ml (note: syrup requires higher doses than capsules, see dosing chart) Capsules: 50 mg, 100 mg, 200 mg Tablets 200mg/600mg	Only for children over 3 yrs	Dose Liquid 19.5mg/kg/day once daily Capsule/tablets 15mg/kg/day once daily Weight more than40kg-600mg once daily	Capsules may be opened and added to food but have very peppery taste; however, can mix with sweet foods or jam to disguise taste Can give with food (but avoid after high fat meals which increase absorption by 50%) Best given at bedtime, especially in the first 2 weeks, to reduce central nervous system side effects Drug interactions
Fixed-dose combination of d4T plus 3TC plus NVP	No liquid available Tablet: d4T6mg+ 3TC30mg+ NVP50mg d4T12mg+ 3TC60mg+ NVP100mg d4T30mg+ 3TC150mg+ NVP200mg	Adults and adolescents	d4T 1mg/kg twice a day 3TC4mg/kg twice a day NVP160-200mg/m2 to a maximum dose of 200mg twice a day	See comments under individual drug components. • A lead-in dose of NVP, at half of the normal daily dosage, is used for 2 weeks to decrease the likelihood of developing rash. • For lead-in dosing, d4T + 3TC + NVP can be used in the morning and d4T + 3TC in the evening. • If the child experiences a rash in the lead-in period, then remain on half the dosage until the rash resolves. Wait no longer than 28 days for the rash to resolve, then seek an alternative regimen.

Fixed-dose combination of AZT plus 3TC plus NVP	AZT60mg + 3TC30mg + NVP50mg AZT300mg + 3TC3150mg + NVP200mg	Adults and adolescents	AZT180-240mg/m^2 twice a day 3TC4mg/kg twice a day NVP160-200mg/M2 twice a day	See comments under individual drugs components N0 food restriction

protease inhibitors				
Lopinavir/ ritonavir, (LPV/r)	Oral solution: 80mg/ml Lopinavir plus 20 mg/ml ritonavir - Heat stable paediatric tablets 100mg Lopinavir plus 25 mg ritonavir Adult tablets 200mg Lopinavir plus 50 mg ritonavir	6 moths of age or older	LPV target dose 230-350mg mg/m^2 twice daily weight-based dosing: 7-15kg: 12mg/kg lopinavir 3 mg/kg ritonavir dose twice daily 15-40 kg: 10 mg/kg lopinavir 2.5 mg/kg ritonavir twice daily Maximum dose: > 40 kg: 400 mg lopinavir 100 mg ritonavir twice daily	Preferably oral solution and capsules should be refrigerated; however, can store at room temperature up to 25`C (77`F) for 2 months; - at temperature >25`C (77`F), drug degrades more rapidly Liquid formulation has low volume but bitter taste Capsules large Capsules should *not* be crushed or opened, but must be swallowed whole Should be taken with food Drug interactions

Name of drug	Formulations	Pharma-cokinetic data available	Age (weight), dose and dose frequency	Other comments
Darunavir (DRV)	Film coated, tablets 75 mg 150 mg 300 mg 400 mg 600 mg	Children aged 6 years or more	Target dose 10 -20 mg /kg twice daily. Maximum dose 600 mg DRV with 100 mg RTV twice daily. Once daily dosing should not be used in pediatric patients,	-should be taken with food -RTV increases metabolism and absorption and should be given with every dose of DRV - The preferred ratio of DRV to RTV is 8:1 . Adding more RTV does not lead to further boosting of DRV levels. - Parents / carers should be warned about potential skin rash - Rarely, DRV has been observed to cause liver problems.
Atazanavir (ATV)	Capsules 100mg 150mg 200mg 300mg	Children aged 3 months to 21 years	Target dose Treatment naive - wt 15kg-<25kg: 150mg ATV/80mgRTV - wt 25kg-<32kg: 200mgATV/100mgRTV - wt 32kg-<39kg: 250mgATV/100mgRTV Treatment experienced - wt 25kg-<32kg: 200mgATV/100mgRTV - wt 32kg-<39kg: 250mgATV/100mgRTV Maximum dose ATV 300mg/RTV100mg once daily	To be used in combination with RTV in pediatric patients. - Recommended for patients aged 6 to <18 years of age - Not to be used in patients less than 3 months of age due to risk of kernicterus. There are insufficient data for patients less than 6 years of age - Dose is based on body weight 8.5 mg /kg for weight 15kg to less than 20kg and 7mg/kg for weight 20kg or more

Ritonavir (RTV)	Liquid 80mg/ml Heat stable tab 100mg	Infant and Children	RTV is used to boost other Protease Inhabitor	- liquid may be taken alone (or) mixed with milk or food but should not be mixed with water (or)other fluid. - liquid is unpalatable and excipient contains 43% alcohol - store tablets at 20-25˚C (range 15-30˚C) Exposure of tablets to high humidity outside tight container for longer than 2 weeks is not recommended. -store liquid at room temperature (20-25˚C) . Do not refrigerate , shake well before each use. Use within 30 days of dispensing. Avoid exposure to excessive heat. Keep cap tightly closed.

Note: meter^2 body surface area calculation: square root of (height in centimeters times weight in kilograms divided by 3600)

Annex 5

Drug formulations and dosages

LAMIVUDINE					
Recommended dosing based on weight-bands for children >6 weeks of age using liquid and adult tablets					
Weight range (kg)		Target dose 4 mg/kg twice daily to a maximum of 150 mg twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	10	mg/ml liquid	3 ml	3 ml
4	4.9	10	mg/ml liquid	3 ml	3 ml
5	5.9	10	mg/ml liquid	3 ml	3 ml
6	6.9	10	mg/ml liquid	4 ml	4 ml
7	7.9	10	mg/ml liquid	4 ml	4 ml
8	8.9	10	mg/ml liquid	4 ml	4 ml
9	9.9	10	mg/ml liquid	4 ml	4 ml
10	10.9	10	mg/ml liquid	6 ml	6 ml
11	11.9	10	mg/ml liquid	6 ml	6 ml
12	13.9	10	mg/ml liquid	6 ml	6 ml
14	16.9	150	mg tablet	½	½
17	19.9	150	mg tablet	½	½
20	24.9	150	mg tablet	1	½
25	29.9	150	mg tablet	1	1
30	34.9	150	mg tablet	1	1

STAVUDINE					
Recommended dosing based on weight-bands for children >6 weeks using liquid and capsules					
Weight range (kg)		Target dose 1 mg/kg twice daily up to 30 mg twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	1	mg/ml liquid	6 ml	6 ml
4	4.9	1	mg/ml liquid	6 ml	6 ml
5	5.9	1	mg/ml liquid	6 ml	6 ml
6	6.9	1	mg/ml liquid	9 ml	9 ml
7	7.9	1	mg/ml liquid	9 ml	9 ml
8	8.9	1	mg/ml liquid	9 ml	9 ml
9	9.9	1	mg/ml liquid	9 ml	9 ml
10	10.9	15	mg capsule	1	1
11	11.9	15	mg capsule	1	1
12	13.9	15	mg capsule	1	1
14	16.9	20	mg capsule	1	1
17	19.9	20	mg capsule	1	1
20	24.9	20	mg capsule	1	1
25	29.9	30	mg capsule	1	1
30	34.9	30	mg capsule	1	1

ZIDOVUDINE					
Recommended dosing based on weight-bands for children >6 weeks using liquid and adult tablets					
Weight range (kg)		Target dose 180 – 240 mg/m^2 twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	10	mg/ml liquid	6 ml	6 ml
4	4.9	10	mg/ml liquid	6 ml	6 ml
5	5.9	10	mg/ml liquid	6 ml	6 ml
6	6.9	10	mg/ml liquid	9 ml	9 ml
7	7.9	10	mg/ml liquid	9 ml	9 ml
8	8.9	10	mg/ml liquid	9 ml	9 ml
9	9.9	10	mg/ml liquid	9 ml	9 ml
10	10.9	10	mg/ml liquid	12 ml	12 ml
11	11.9	10	mg/ml liquid	12 ml	12 ml
12	13.9	10	mg/ml liquid	12 ml	12 ml
14	16.9	300	mg tablet	½	½
17	19.9	300	mg tablet	½	½
20	24.9	300	mg tablet	1	½
25	29.9	300	mg tablet	1	1
30	34.9	300	mg tablet	1	1

ZIDOVUDINE					
Recommended dosing based on weight-bands for children >6 weeks using liquid and capsules					
Weight range (kg)		Target dose 180 – 240 mg/m^2 twice daily		Dose (ml or capsules)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	10	mg/ml liquid	6 ml	6 ml
4	4.9	10	mg/ml liquid	6 ml	6 ml
5	5.9	10	mg/ml liquid	6 ml	6 ml
6	6.9	10	mg/ml liquid	9 ml	9 ml
7	7.9	10	mg/ml liquid	9 ml	9 ml
8	8.9	100	mg capsule	1	1
9	9.9	100	mg capsule	1	1
10	10.9	100	mg capsule	1	1
11	11.9	100	mg capsule	1	1
12	13.9	100	mg capsule	1	1
14	16.9	100	mg capsule	2	1
17	19.9	100	mg capsule	2	1
20	24.9	100	mg capsule	2	2
25	29.9	100	mg capsule	2	2
30	34.9	100	mg capsule	3	3

ZIDOVUDINE					
Recommended dosing based on weight-bands for children >6 weeks using paediatric tablets					
Weight range (kg)		Target dose 180 – 240 mg/m^2 twice daily		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	60	mg tablet	1	1
4	4.9	60	mg tablet	1	1
5	5.9	60	mg tablet	1	1
6	6.9	60	mg tablet	1.5	1.5
7	7.9	60	mg tablet	1.5	1.5
8	8.9	60	mg tablet	1.5	1.5
9	9.9	60	mg tablet	1.5	1.5
10	10.9	60	mg tablet	2	2
11	11.9	60	mg tablet	2	2
12	13.9	60	mg tablet	2	2
14	16.9	60	mg tablet	2.5	2.5
17	19.9	60	mg tablet	2.5	2.5
20	24.9	60	mg tablet	3	3
25	29.9	300	mg tablet	1	1
30	34.9	300	mg tablet	1	1

ABACAVIR					
Recommended dosing based on weight-bands for children >6 weeks using liquid and adult tablets					
Weight range (kg)		Target dose <16 years or <37.5 kg: 8 mg/kg/dose given twice daily Maximum dose >16 years or ≥37.5 kg: 300 mg/dose given twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	20	mg/ml liquid	3 ml	3 ml
4	4.9	20	mg/ml liquid	3 ml	3 ml
5	5.9	20	mg/ml liquid	3 ml	3 ml
6	6.9	20	mg/ml liquid	4 ml	4 ml
7	7.9	20	mg/ml liquid	4 ml	4 ml
8	8.9	20	mg/ml liquid	4 ml	4 ml
9	9.9	20	mg/ml liquid	4 ml	4 ml
10	10.9	20	mg/ml liquid	6 ml	6 ml
11	11.9	20	mg/ml liquid	6 ml	6 ml
12	13.9	20	mg/ml liquid	6 ml	6 ml
14	16.9	300	mg tablet	½	½
17	19.9	300	mg tablet	½	½
20	24.9	300	mg tablet	1	½
25	29.9	300	mg tablet	1	1
30	34.9	300	mg tablet	1	1

ABACAVIR

Recommended dosing based on weight-bands for children >6 weeks using paediatric tablets

Weight range (kg)		Target dose <16 years or <37.5 kg: 8 mg/kg/dose given twice daily Maximum dose >16 years or ≥37.5 kg: 300 mg/dose given twice daily		Dose (tablet)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	60	mg tablet	1	1
4	4.9	60	mg tablet	1	1
5	5.9	60	mg tablet	1	1
6	6.9	60	mg tablet	1.5	1.5
7	7.9	60	mg tablet	1.5	1.5
8	8.9	60	mg tablet	1.5	1.5
9	9.9	60	mg tablet	1.5	1.5
10	10.9	60	mg tablet	2	2
11	11.9	60	mg tablet	2	2
12	13.9	60	mg tablet	2	2
14	16.9	60	mg tablet	2.5	2.5
17	19.9	60	mg tablet	2.5	2.5
20	24.9	60	mg tablet	3	3
25	29.9	300	mg tablet	1	1
30	34.9	300	mg tablet	1	1

DIDANOSINE

Recommended dosing based on weight-bands for children >3 months using liquid and chewable tablets

Weight range (kg)		Target dose 3 months to <13 years: 90–120 mg/m^2/dose twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	10	mg/ml liquid	NR	NR
4	4.9	10	mg/ml liquid	NR	NR
5	5.9	10	mg/ml liquid	3 ml	3 ml
6	6.9	10	mg/ml liquid	5 ml	5 ml
7	7.9	10	mg/ml liquid	5 ml	5 ml
8	8.9	10	mg/ml liquid	5 ml	5 ml
9	9.9	10	mg/ml liquid	5 ml	5 ml
10	10.9	10	mg/ml liquid	6 ml	6 ml
11	11.9	10	mg/ml liquid	6 ml	6 ml
12	13.9	10	mg/ml liquid	6 ml	6 ml
14	16.9	25	mg tablet	4	3
17	19.9	25	mg tablet	4	3
20	24.9	25	mg tablet	4	4
25	29.9	25	mg tablet	5	5
30	34.9	25	mg tablet	5	5

DIDANOSINE

Recommended dosing based on weight-bands for children >3 months using chewable tablets

Weight range (kg)		Target dose 3 months to <13 years: 90–120 mg/m²/dose twice daily		Dose (tablet)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	25	mg tablet	NR	NR
4	4.9	25	mg tablet	NR	NR
5	5.9	25	mg tablet	2	2
6	6.9	25	mg tablet	3	2
7	7.9	25	mg tablet	3	2
8	8.9	25	mg tablet	3	2
9	9.9	25	mg tablet	3	2
10	10.9	25	mg tablet	3	3
11	11.9	25	mg tablet	3	3
12	13.9	25	mg tablet	3	3
14	16.9	25	mg tablet	4	3
17	19.9	25	mg tablet	4	3
20	24.9	25	mg tablet	4	4
25	29.9	25	mg tablet	5	5
30	34.9	25	mg tablet	5	5

Note: 25 mg chewable tablets can be substituted with other strengths to the same mg amount but each a.m. and p.m. dose must always be made up of at least two tablets.

NR not recommended

DIDANOSINE

Recommended once-daily dosing based on weight-bands using enteric-coated capsules

Weight range (kg)		Target dose 240–300 mg/m²/day		Dose (ml or tablets)
Bottom	Top	Formulation		a.m. or p.m.
3	3.9	NR		NR
4	4.9	NR		NR
5	5.9	NR		NR
6	6.9	NR		NR
7	7.9	NR		NR
8	8.9	NR		NR
9	9.9	NR		NR
10	10.9	125	mg EC capsule	1
11	11.9	125	mg EC capsule	1
12	13.9	125	mg EC capsule	1
14	16.9	200	mg EC capsule	1
17	19.9	200	mg EC capsule	1
20	24.9	125	mg EC capsule	2
25	29.9	125	mg EC capsule	2
30	34.9	125	mg EC capsule	2

NR not recommended

EFAVIRENZ				
Recommended maintenance dosing based on weight-bands				
Weight range (kg)		Target dose 15 mg/kg/day (capsule/tablet) Weight >40 kg: 600 mg once daily		Dose (tablets)
Bottom	Top	Formulation		Once daily
3	3.9	NR		NR
4	4.9	NR		NR
5	5.9	NR		NR
6	6.9	NR		NR
7	7.9	NR		NR
8	8.9	NR		NR
9	9.9	NR		NR
10	10.9	200	mg tablet	1
11	11.9	200	mg tablet	1
12	13.9	200	mg tablet	1
14	16.9	200	mg tablet	1.5
17	19.9	200	mg tablet	1.5
20	24.9	200	mg tablet	1.5
25	29.9	200	mg tablet	2
30	34.9	200	mg tablet	2

NR not recommended

NEVIRAPINE					
Recommended maintenance dose based on weight-bands for children >6 weeks using liquid and adult tablets					
Weight range (kg)		Target dose 160 – 200 mg/m^2 to max 200 mg twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	10	mg/ml liquid	5 ml	5 ml
4	4.9	10	mg/ml liquid	5 ml	5 ml
5	5.9	10	mg/ml liquid	5 ml	5 ml
6	6.9	10	mg/ml liquid	8 ml	8 ml
7	7.9	10	mg/ml liquid	8 ml	8 ml
8	8.9	10	mg/ml liquid	8 ml	8 ml
9	9.9	10	mg/ml liquid	8 ml	8 ml
10	10.9	10	mg/ml liquid	10 ml	10 ml
11	11.9	10	mg/ml liquid	10 ml	10 ml
12	13.9	10	mg/ml liquid	10 ml	10 ml
14	16.9	200	mg tablet	1	½
17	19.9	200	mg tablet	1	½
20	24.9	200	mg tablet	1	½
25	29.9	200	mg tablet	1	1
30	34.9	200	mg tablet	1	1

NEVIRAPINE					
Recommended maintenance dose based on weight-bands for children >6 weeks using paediatric and adult tablets					
Weight range (kg)		Target dose 160 – 200 mg/m^2 to max 200 mg twice daily		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	50	mg tablet	1	1
4	4.9	50	mg tablet	1	1
5	5.9	50	mg tablet	1	1
6	6.9	50	mg tablet	1.5	1.5
7	7.9	50	mg tablet	1.5	1.5
8	8.9	50	mg tablet	1.5	1.5
9	9.9	50	mg tablet	1.5	1.5
10	10.9	50	mg tablet	2	2
11	11.9	50	mg tablet	2	2
12	13.9	50	mg tablet	2	2
14	16.9	50	mg tablet	2.5	2.5
17	19.9	50	mg tablet	2.5	2.5
20	24.9	50	mg tablet	3	3
25	29.9	200	mg tablet	1	1
30	34.9	200	mg tablet	1	1

LOPINAVIR/RITONAVIR					
Recommended dosing based on weight-bands for children >6 weeks using liquid					
Weight range (kg)		Target dose 230 – 350 mg/m^2 twice daily		Dose (ml)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	80 mg LPV/20 mg RTV	ml liquid	1 ml	1 ml
4	4.9	80 mg LPV/20 mg RTV	ml liquid	1.5 ml	1.5 ml
5	5.9	80 mg LPV/20 mg RTV	ml liquid	1.5 ml	1.5 ml
6	6.9	80 mg LPV/20 mg RTV	ml liquid	1.5 ml	1.5 ml
7	7.9	80 mg LPV/20 mg RTV	ml liquid	1.5 ml	1.5 ml
8	8.9	80 mg LPV/20 mg RTV	ml liquid	1.5 ml	1.5 ml
9	9.9	80 mg LPV/20 mg RTV	ml liquid	1.5 ml	1.5 ml
10	10.9	80 mg LPV/20 mg RTV	ml liquid	2 ml	2 ml
11	11.9	80 mg LPV/20 mg RTV	ml liquid	2 ml	2 ml
12	13.9	80 mg LPV/20 mg RTV	ml liquid	2 ml	2 ml
14	16.9	80 mg LPV/20 mg RTV	ml liquid	2.5 ml	2.5 ml
17	19.9	80 mg LPV/20 mg RTV	ml liquid	2.5 ml	2.5 ml
20	24.9	80 mg LPV/20 mg RTV	ml liquid	3 ml	3 ml
25	29.9	80 mg LPV/20 mg RTV	ml liquid	3.5 ml	3.5 ml
30	34.9	80 mg LPV/20 mg RTV	ml liquid	4 ml	4 ml

LOPINAVIR/RITONAVIR					
Recommended dosing based on weight-bands for children >6 weeks using paediatric tablets					
Weight range (kg)		Target dose 230 – 350 mg/m^2 twice daily		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	100 mg LPV/25 mg RTV	tablet	NR	NR
4	4.9	100 mg LPV/25 mg RTV	tablet	NR	NR
5	5.9	100 mg LPV/25 mg RTV	tablet	NR	NR
6	6.9	100 mg LPV/25 mg RTV	tablet	NR	NR
7	7.9	100 mg LPV/25 mg RTV	tablet	NR	NR
8	8.9	100 mg LPV/25 mg RTV	tablet	NR	NR
9	9.9	100 mg LPV/25 mg RTV	tablet	NR	NR
10	10.9	100 mg LPV/25 mg RTV	tablet	2	1
11	11.9	100 mg LPV/25 mg RTV	tablet	2	1
12	13.9	100 mg LPV/25 mg RTV	tablet	2	1
14	16.9	100 mg LPV/25 mg RTV	tablet	2	2
17	19.9	100 mg LPV/25 mg RTV	tablet	2	2
20	24.9	100 mg LPV/25 mg RTV	tablet	2	2
25	29.9	100 mg LPV/25 mg RTV	tablet	3	3
30	34.9	100 mg LPV/25 mg RTV	tablet	3	3

Note: Children 14 – 24.9 kg can be dosed with adult tabs (200 mg LPV/50 mg RTV), 1 tab am and 1 tab pm.
Children 25 – 34.9 kg can be dosed with adult tabs (200 mg LPV/50 mg RTV), 2 tabs am and 1 tab pm.

AZT PLUS 3TC					
Recommended dosing based on weight-bands					
Weight range (kg)		Target dose as for individual components		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	60/30	tablet	1	1
4	4.9	60/30	tablet	1	1
5	5.9	60/30	tablet	1	1
6	6.9	60/30	tablet	1.5	1.5
7	7.9	60/30	tablet	1.5	1.5
8	8.9	60/30	tablet	1.5	1.5
9	9.9	60/30	tablet	1.5	1.5
10	10.9	60/30	tablet	2	2
11	11.9	60/30	tablet	2	2
12	13.9	60/30	tablet	2	2
14	16.9	60/30	tablet	2.5	2.5
17	19.9	60/30	tablet	2.5	2.5
20	24.9	60/30	tablet	3	3
25	29.9	300/150	tablet	1	1
30	34.9	300/150	tablet	1	1

AZT PLUS 3TC PLUS NVP					
Recommended dosing based on weight-bands					
Weight range (kg)		Target dose as for individual components		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	60/30/50	tablet	1	1
4	4.9	60/30/50	tablet	1	1
5	5.9	60/30/50	tablet	1	1
6	6.9	60/30/50	tablet	1.5	1.5
7	7.9	60/30/50	tablet	1.5	1.5
8	8.9	60/30/50	tablet	1.5	1.5
9	9.9	60/30/50	tablet	1.5	1.5
10	10.9	60/30/50	tablet	2	2
11	11.9	60/30/50	tablet	2	2
12	13.9	60/30/50	tablet	2	2
14	16.9	60/30/50	tablet	2.5	2.5
17	19.9	60/30/50	tablet	2.5	2.5
20	24.9	60/30/50	tablet	3	3
25	29.9	300/150/200	tablet	1	1
30	34.9	300/150/200	tablet	1	1

D4T PLUS 3TC					
Recommended dosing based on weight-bands					
Weight range (kg)		Target dose as for individual components		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	6/30	mg tablet	1	1
4	4.9	6/30	mg tablet	1	1
5	5.9	6/30	mg tablet	1	1
6	6.9	6/30	mg tablet	1.5	1.5
7	7.9	6/30	mg tablet	1.5	1.5
8	8.9	6/30	mg tablet	1.5	1.5
9	9.9	6/30	mg tablet	1.5	1.5
10	10.9	6/30	mg tablet	2	2
11	11.9	6/30	mg tablet	2	2
12	13.9	6/30	mg tablet	2	2
14	16.9	6/30	mg tablet	2.5	2.5
17	19.9	6/30	mg tablet	2.5	2.5
20	24.9	6/30	mg tablet	3	3
25	29.9	30/150	mg tablet	1	1
30	34.9	30/150	mg tablet	1	1

D4T PLUS 3TC PLUS NVP					
Recommended dosing based on weight-bands					
Weight range (kg)		Target dose as for individual components		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	6/30/50	tablet	1	1
4	4.9	6/30/50	tablet	1	1
5	5.9	6/30/50	tablet	1	1
6	6.9	6/30/50	tablet	1.5	1.5
7	7.9	6/30/50	tablet	1.5	1.5
8	8.9	6/30/50	tablet	1.5	1.5
9	9.9	6/30/50	tablet	1.5	1.5
10	10.9	6/30/50	tablet	2	2
11	11.9	6/30/50	tablet	2	2
12	13.9	6/30/50	tablet	2	2
14	16.9	6/30/50	tablet	2.5	2.5
17	19.9	6/30/50	tablet	2.5	2.5
20	24.9	6/30/50	tablet	3	3
25	29.9	30/150/200	tablet	1	1
30	34.9	30/150/200	tablet	1	1

ABC PLUS AZT PLUS 3TC					
Recommended dosing based on weight-bands					
Weight range (kg)		Target dose as for individual components		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	60/60/30	tablet	1	1
4	4.9	60/60/30	tablet	1	1
5	5.9	60/60/30	tablet	1	1
6	6.9	60/60/30	tablet	1.5	1.5
7	7.9	60/60/30	tablet	1.5	1.5
8	8.9	60/60/30	tablet	1.5	1.5
9	9.9	60/60/30	tablet	1.5	1.5
10	10.9	60/60/30	tablet	2	2
11	11.9	60/60/30	tablet	2	2
12	13.9	60/60/30	tablet	2	2
14	16.9	60/60/30	tablet	2.5	2.5
17	19.9	60/60/30	tablet	2.5	2.5
20	24.9	60/60/30	tablet	3	3
25	29.9	300/300/150	tablet	1	1
30	34.9	300/300/150	tablet	1	1

ABC PLUS 3TC					
Recommended dosing based on weight-bands					
Weight range (kg)		Target dose as for individual components		Dose (tablets)	
Bottom	Top	Formulation		a.m.	p.m.
3	3.9	60/30	tablet	1	1
4	4.9	60/30	tablet	1	1
5	5.9	60/30	tablet	1	1
6	6.9	60/30	tablet	1.5	1.5
7	7.9	60/30	tablet	1.5	1.5
8	8.9	60/30	tablet	1.5	1.5
9	9.9	60/30	tablet	1.5	1.5
10	10.9	60/30	tablet	2	2
11	11.9	60/30	tablet	2	2
12	13.9	60/30	tablet	2	2
14	16.9	60/30	tablet	2.5	2.5
17	19.9	60/30	tablet	2.5	2.5
20	24.9	60/30	tablet	3	3
25	29.9	600/300 [i]	tablet	½	½
30	34.9	600/300 [i]	tablet	½	½

(i) Currently, there is no experience in using the 600/300 tablet to provide 300/150 twice-daily dosing. Consider halving the 600/300 tablet and giving one half tablet twice daily, or give one tablet daily. Adult ABC/3TC FDC tablets are not scored; a tablet cutter would be required to divide these tablets.

Annex 6

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