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缅甸联邦第一特区卫生部

The Union of Myanmar, SR(1) Department of Health

HIV Infection

Standard Operating Procedure (SOP)

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HIV Infection

Clinical Diagnosis

Revised WHO clinical staging of HIV / AIDS for infants and children with established

HIV infection

This staging system is designed to provide guidance on when to start, stop or substitute antiretroviral therapy in HIV-infected children.

WHO clinical staging of HIV disease in children
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
• Moderate unexplained malnutrition* not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (above 37.5ºC intermittent or constant, for longer than one month) • Persistent oral candida (outside first 6-8 weeks of life) • Oral hairy leukoplakia • Acute necrotizing ulcerative gingivitis/periodontitis • Lymph node TB • Pulmonary tuberculosis • Severe recurrent presumed bacterial pneumonia • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease including bronchiectasis • Unexplained anaemia (<8 g/dl), neutropenia (<0.5x10'/L) or chronic thrombocytopenia (<50x10^9/L)

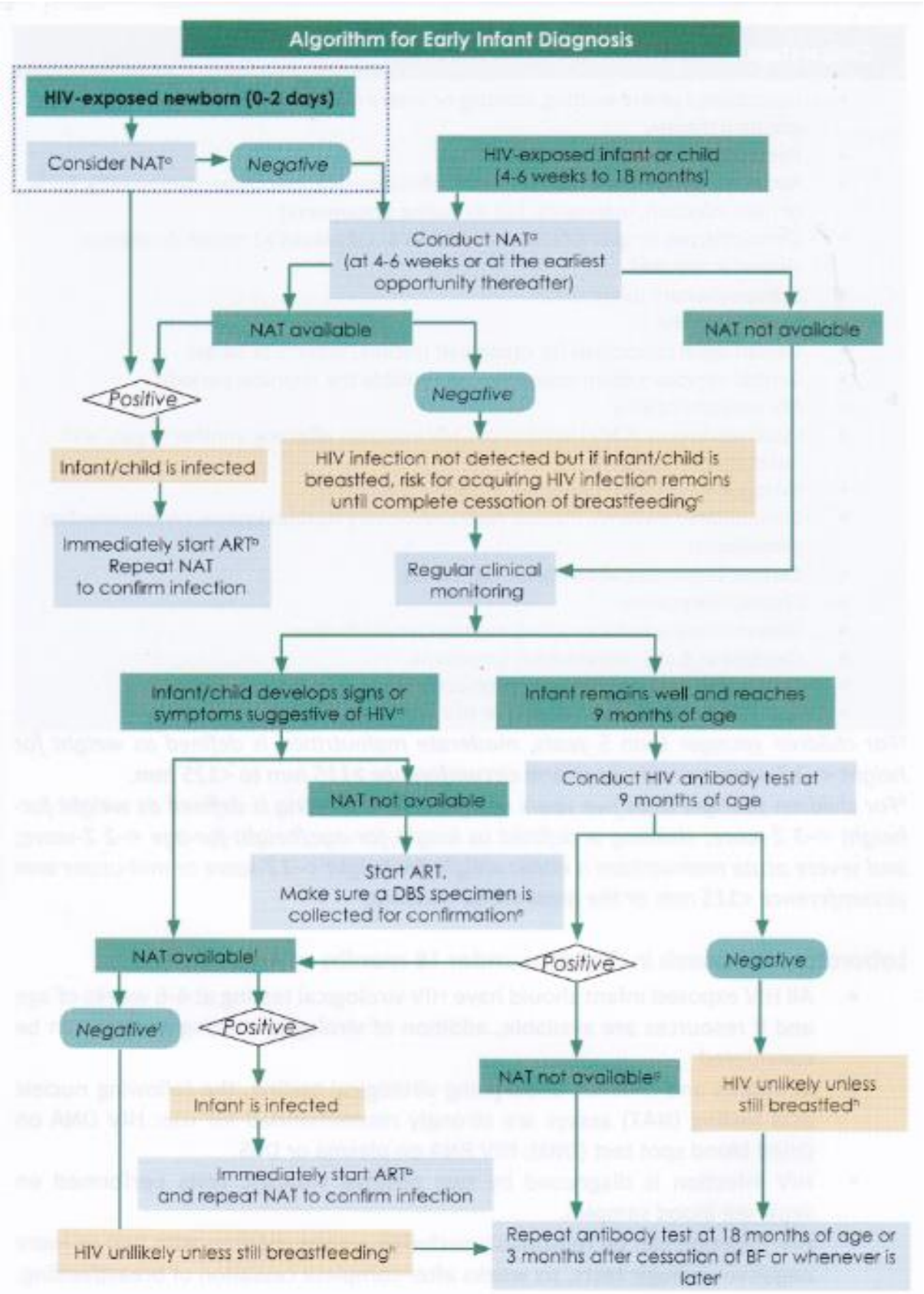
Clinical stage 4
Unexplained severe wasting, stunting or severe malnutrition" not responding to standard therapy
Pneumocystis jiroveci pneumonia
Recurrent severe presumed bacterial infections (e.8.empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection; (orolabial or cutaneous >1 month duration or visceral at any site)
Extrapulmonary tuberculosis
Kaposi sarcoma
Oesophageal candidiasis (or candida of trachea, bronchi or lungs)
Central nervous system toxoplasmosis (outside the neonatal period)
HIV encephalopathy
Cytomegalovirus (CMV) retinitis or CMV infection affecting another organ, with onset at age >1 month
Extrapulmonary cryptococcosis including meningitis
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
Chronic Cryptosporidiosis (with diarrhoea)
Chronic lsosporiasis
Disseminated non-tuberculous mycobacterial infection
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
HIV-associated cardiomyopathy or HIV-associated nephropathy

For children younger than 5 years, moderate malnutrition is defined as weight for height <-2 2-score or mid-upper arm circumference ≥115 mm to <125 mm.

For children younger than five years of age, severe wasting is defined as weight-for-height <-3 2-score; stunting is defined as length-for-age/height-for-age <-2 2-score, and severe acute malnutrition is either weight for height <-3 2-score or mid-upper arm circumference <115 mm or the presence of oedema.

Laboratory Diagnosis in Children under 18 months of Age

- All HIV exposed infant should have HIV virological testing at 4-6 weeks of age and if resources are available, addition of virological testing at birth can be considered
- In infants and children undergoing virological testing, the following nucleic acid testing (NAT) assays are strongly recommended for use: HIV DNA on Dried blood spot test (DBS); HIV RNA on plasma or DBS.
- HIV infection is diagnosed by two positive virologic tests performed on separate blood samples.
- HIV infection can be reasonably excluded among children with two or more negative virologic tests, six weeks after complete cessation of breastfeeding


Algorithm for Early Infant Diagnosis
HIV-exposed newborn (0-2 days)
Consider NAT[c]
Negative
HIV-exposed infant or child (4-6 weeks to 18 months)
Conduct NAT[a] (at 4-6 weeks or at the earliest opportunity thereafter)
NAT available
NAT not available
Positive
Negative
Infant/child is infected
HIV infection not detected but if infant/child is breastfed, risk for acquiring HIV infection remains until complete cessation of breastfeeding[c]
Immediately start ART[b] Repeat NAT to confirm infection
Regular clinical monitoring
Infant/child develops signs or symptoms suggestive of HIV[e]
Infant remains well and reaches 9 months of age
NAT not available
Conduct HIV antibody test at 9 months of age
Start ART, Make sure a DBS specimen is collected for confirmation[e]
NAT available[f]
Positive
Negative
Negative[f]
Positive
NAT not available[g]
HIV unlikely unless still breastfed[h]
Infant is infected
Immediately start ART[b] and repeat NAT to confirm infection
HIV unlikely unless still breastfeeding[h]
Repeat antibody test at 18 months of age or 3 months after cessation of BF or whenever is later[i]

Important Notes:

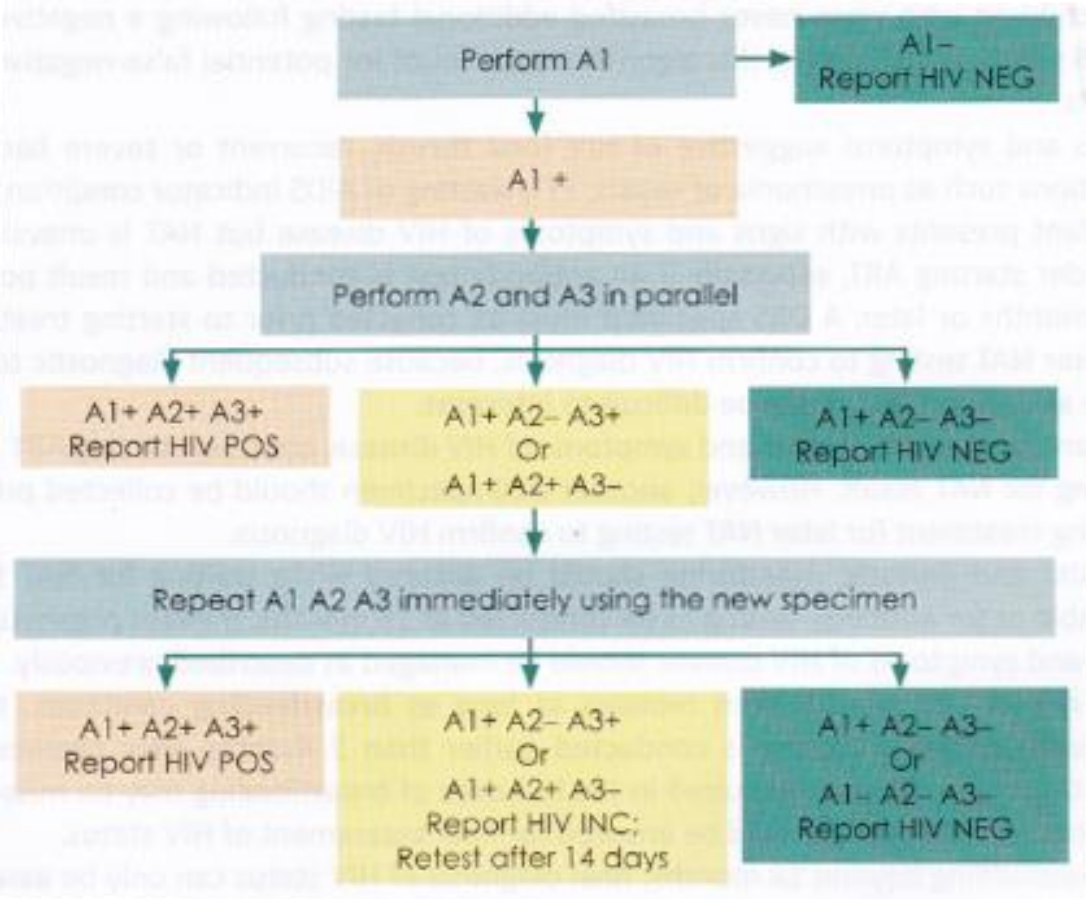
[a]Based on these revised Guidelines addition of Nucleic Acid Testing (NAT) at birth tothe existing testing algorithm can be considered.
[b]Start ART, without delay. At the same time, retest to confirm infection. As maternaltreatment is scaled up and TCT transmission rates decrease, false-positive resultsare expected to increase and retesting after a frst positive NAT is important to avoidunnecessarily treatment, particularly in settings with lower transmission rates. lf thesecond test is negative, a third NAT should be done before interrupting ART.
[c]For children who were never breastfed additional testing following a negative NAT at 4-6 weeks is included in this algorithm to account for potential false-negative NAT results.
[d]Signs and symptoms suggestive of HlV (oral thrush, recurrent or severe bacterialinfections such as pneumonia or sepsis, FTT/wasting or AlDS indicator condition).
[e]If infant presents with signs and symptoms of HlV disease but NAT is unavailableconsider starting ART, especially if an antibody test is conducted and result positiveat 9 months or later, A DBS specimen must be collected prior to starting treatmentfor later NAT testing to confirm HlV diagnosis, because subsequent diagnostic testingwhile already on ART might be difficult to interpret.
[f]If infant presents with signs and symptoms of HlV disease, consider starting ART whilewaiting for NAT result. However, another DBS specimen should be collected prior tostarting treatment for later NAT testing to confrm HlV diagnosis.
[g]Regular and periodic monitoring should be ensured while waiting for NAT to beavailable or for antibody testing to be conducted at 18 months. lf infant presents withsigns and symptoms of HlV disease should be managed as described previously.
[h]The risk of HlV transmission remains as long as breastfeeding continues. If the 9 months antibody testing is conducted earlier than 3 months after cessation ofbreastfeeding, infections acquired in the last days of breastfeeding may be missed soretesting at 18 months should be ensured for final assessment of HIV status.
[i]If breastfeeding beyond 18 months, final diagnosis of HlV status can only be assessedat the end of breastfeeding. lf breastfeeding ends before 18 months, final diagnosis of HIV status with antibody testing can only be assessed at 18 months. Antibody testingshould be undertaken at least 3 months after cessation of breastfeeding (to allowfor development of HlV antibodies). For infants <18 months of age positive antibodytesting requires NAT to confrm infection. lf infant is >18 months, negative antibodytesting confirms infant is uninfected; positive antibody testing confirms infant is infected.

HIV diagnosis in Children 18 months of age and older

Every initial positive antibody assay (A1) requires confirmation with 2nd and 3rd testsusing a different assay techniques (A2) and (A3)

Recommended rapid test kits for 3-assay HlV Testing Strategy are:

- A1 = Determine HIV-1/2 (D)ICT
- A2 = Uni-Gold HIV(UG)ICT
- A3 = HIV 1/2 STAT-Pack (SP)ICT



Management of Children Born to HIV-infected Mothers

Ultimate goal

- To maintain health by providing access to comprehensive care and support services

Comprehensive care includes

- Antiretroviral therapy for treatment of established HIV infection
- Prevention of perinatal transmission of HIV
- Prevention (prophylaxis) and treatment of opportunistic infections (OIs)
- Counseling and testing
- Psycho-social and nutritional support

Infant feeding

- ***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 riskof HIV to infants through breastfeeding with the need for minimising the riskof other causes of morbidity and mortality through not breastfeeding

- ***Provide*** counselling and information about the risks and benefits of variousinfant feeding options based on locally feasible and acceptable feedingpractices
- ***Recommend*** infant feeding recommended for HlV infected women is tochoose between formula feeding or exclusive breastfeeding. Breastfeedingis a preferred option; exclusive breastfeeding for 6 months, introducing complementary food thereafter, continuing breastfeeding for 12 months,weaninggradually within 1 month.Formula feeding without any breastfeeding can be chosen only if all the following conditions are met:

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 formula milk to support normal growth and development of the infant and
c. The mother or caregiver can prepare it cleanly and frequently enoughso that it is safe and carries a low risk of diarrhea and malnutrition; and
d. The mother or caregiver can, in the first six months, exclusively giveinfant formula milk; and
e. The family is supportive of this practice; and
f. The mother orcaregiver can access health care that offers comprehensive child health services.

Cotrimoxazole Prophylaxis for Pneumocystis (Carinil) Jirovecii Pneumonia (PCP)

- Co-trimoxazole prophylaxis is recommended for HIV-exposed infants from 4 to 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete cessation of breastfeeding.
- Co-trimoxazole prophylaxis is recommended for infants. children, and adolescents with HIV, irrespective of clinical and immune conditions. Priority should be given to all children less than 5 years old regardless of CD4 cellcount or clinical stage, and children with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and/or those with CD4 s350 cells/mm^3.
- Co-trimoxazole prophylaxis may be discontinued for children 5 years of age and older who are clinically stable and/or virally suppressed on ART for atleast 6 months and with a CD4 count >350 cells/mm^3.

Management of HIV-infected children

- 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.
- Assess whether the child fulfis the criteria for starting ART
- Starting ART is not an emergency but once started the treatment must begiven on time every day, Non-adherence to treatment is the main reason for treatment failure.
- Assess the family situation including, but not limited to, the number ofpersons with or at risk for HIV infection and their current health/treatmentstatus.
- 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 HlV diagnosis within the family (whether thechild knows his/her diagnosis, whether anyone else knows, and if the child knows the parent[s]' HlV status).
- Assess the financial status of the family, including their ability to pay for transportation to the clinic, afford adequate food/nutritional supplements forthe child, pay for any treatment needed and whether they have a refrigeratol for keeping ARVs that need to be stored at a low temperature, if required.

HIV Staging in Children Using Clinical and lmmunological Criteria

Clinical criteria

Table 8.15 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 8.16 lmmunological criteria (CD4)

WHO classification ofHiV-associated immunodeficiency using CD4				
	Age-related CD4 values			
	<11 months (%)	12-35 months (%)	36-59 months (%)	25 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 8.17 Summary of recommendations on when to start ART in adolescent, children and infants

Adolescents	**Initiate ART regardless of WHO clinical stage and at any CD4 count**. As a priority, initiate those: • Severe HiV clinical disease (WHO clinical stage 3 or 4) • CD4 count ≤350 cells/mm³
Children andinfants	Initiate ART regardless of WHO clinical stage or at any CD4 count. As a priority, initiate those: • All children under 2 years of age • Children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 mm^3 or CD4 percentage <25% • Children 5 years of age and older with WHO clinical stage 3 or4 or CD4 count ≤350 mm^3

Table 8.18 What to start: first-line ART

First-line ARTregimens for adolescents and children

First-line ART	Preferred first-line regimens	Alternative first-line regimens
Adolescents	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV TDF + 3TC(Or FTC) + DTG[2] ABC + 3TC (or FTC) + EFV
Children 3 to <10 years	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + EFV (or NVP)
Children <3 years	ABC (or AZT) + 3TC + LPV/r	ABC (Or AZT) + 3TC + NVP **Special circumstances**[b] ABC or AZT + 3TC + RAL

[a]Safety and effcacy data on the use of DTG in people with HIV/TB coinfection andadolescents younger than 12 years of age are not yet available.

[b]Special circumstances may include situations where preferred or alternative regimensmay not be available or suitable because of significant toxicities, anticipated drug-druginteractions, drug procurement and supply management issues or for other reasons. (3TC lamivudine, ABC abacavir, AZT zidovudine, DRV darunavir, DTG dolutegravir, EFV efavirenz, FTC emtricitabine, LPV lopinavir, NVP nevirapine, r ritonavir, TDF tenofovir.)

Table 8.19 Recommended laboratory monitoring of ART

Phase of HIV management	Recommended	Desirable
HIV diagnosis	- HIV testing (serology for children 18 months or older, Early Infant Diagnosis (ElD) for children younger than 18 months) - CD4 cell count - TB symptom screening	HBV (HBsAg) serology[3] HCC serology
Follow-up before ART	CD4 cell count (every 6-12 months in circumstances where ART initiation is delayed)	
ART initiation	CD4 cell count	Haemoglobin test for starting AZT[b] Blood pressure measurement Serum creatinine and estimated glomerular filtration rate (eGFR) orstarting TDF[c] Alanine aminotransferase for NVP[f]
Receiving ART	HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter). If routine viral load is notavailable, targeted viral load testing is recommended. CD4 cell count every 6 monthsuntil patients are stable on ART	
Suspected treatment failure	Serum creatinine and eGFR for TDF[C]	HBV (HBsAg) serology[a.d] (before switching ART regimen if this testingwas not done or if the result wasnegative at baseline and the patientwas not vaccinated thereafter)

[a]If feasible, HBsAg testing should be performed at baseline to identify people with HIV and HBV coinfection and who should therefore initiate TDF-containing ART.

[b]Among children and adolescents with a high risk of adverse events associated with AZT (low CD4 or low BMI).

[c]Among people with a high risk of adverse events associated with TDF: underlying renal disease, older age group, low body mass index (BMl), diabetes, hypertension and concomitant use of a boosted PI or potential nephrotoxic drugs.

[d]For HIV/HBV coinfected individuals who are already using TDF-containing regimens and develop ART failure, this NRTl should be maintained regardless of the selected second-line regimen

Table 8.20 WHO definitions of clinical, immunological and virological failure for the decision to switch ART regimens

Failure	Definitions
Clinical failure	**Adolescents** New or recurrent clinical event indicating severeimmunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment **Children** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinicalcondition with the exception of TB) after 6 months of effective treatment
Immunological failure	**Adolescents** CD4 count at or below 250 cells/mm³ following clinical failureor Persistent CD4 levels below 100 cells/mm³ **Children** ***Younger than 5 years*** Persistent CD4 levels below 200 cells/mm^3 ***Older than 5 years*** Persistent CD4 levels below 100 cells/mm^3
Virological failure	Viral load above 1000 copies/ml based on two consecuti veviral load measurements within 2-3 months, with adherencesupport following the frst viral load test

What ART regimen to switch to (second line ART)

Table 8.21 Preferred second-line ART regimens for adolescents and children

Population		Failing first-lineregimen	Preferred second-line regimen	Alternative second.line regimens
Adolescents		2 NRTIS + EFV (or NVP)	2 NRTIs[b] + ATV/r or LPV/r	2 NRTIs[b]+ DRV/r[c] 2 NRTIs[b] + DTG[c]
		2 NRTIs + DTG		
Children	Less than 3 years	2 NRTIs + LPV/r	2NRTIs[b] + RAL	Maintain thefailing Lpv/r-based regimen and switcht 2 NRTIs[b] + EFV at 3 years of age
		2 NRTIs + NVP	2NRTIs[b] + LPV/r	2NRTIs[b] + RAL[d]
	3 years toless than 10 years	2 NRTIS + LPV/r[a]	2 NRTIs[b] + EFV	2NRTIs[b] + RAL[d]
		2 NRTIS + EFV (or NVP)	2 NRTIs[b] + LPW/r	2 NRTIs[b] + ATV/r[d]

[a]ATV/r can be used as an alternative PI for children older than 3 months of age.
[b]If ABC+ 3TC or TDF + 3TC (or FTC) was used in the first-line failing regimen, AZT + 3TC should beused in second-line and vice versa.
[c]RAL + LPV/r can be used as an alternative second-line regimen in adults and adolescents.
[d]DRV/'r can be used as an alternative Pl option in special situations.
[e]2 NRTls + DTG can also be used as an alternative second-line especially for patients failing with first-line regimen not including DTG.
3TC lamivudine, ABC abacavir, ATVatazanavir, A2T zidovudine, DTG dolutegravir, EFVefavirenz, FTC emtricitabine, LPV lopinavir, NRTl nucleoside reverse-transcriptase inhibitor, NVP nevirapine PI protease inhibitor, ror RTVritonavir, RAL raltegravir.