CHAPTER 9

HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS

9.1 HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS

B20–24

Comprehensive guidelines are available for ART and the care of children with HIV infection in the 2023 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy and Breastfeeding, Adolescents, Children, Infants and Neonates.[1]

DESCRIPTION

Human Immunodeficiency Virus (HIV) is a retrovirus infecting immune cells, especially CD4 T-lymphocytes. In advanced HIV disease, the body loses its ability to fight infections, and this stage is characterised by severe damage to organs, opportunistic infections, malignancies and very low CD4 counts.

In infants, most infections are vertically transmitted, but in adolescents and adults, sexual transmission is the usual route for new infections.

Infants born to mothers with HIV may be:

- HIV-infected.
- 'HIV-exposed':
  - At risk of being/becoming HIV-infected.
  - HIV-uninfected.

For the purpose of the ART guidelines:

- Children (< 10 years and < 30 kg): follow the Paediatric Antiretroviral Therapy (ART) Guidelines.
- Adolescents (10–19 years): follow the Adult and Adolescent ART Guidelines.

DIAGNOSTIC CRITERIA

All infants/children accessing care should have their HIV status determined.

- Patients with a previously positive HIV test and on ART should not be re-tested.
- Where mothers tested negative during pregnancy, maternal HIV status should be determined three-monthly whilst breastfeeding.

Confirmation of HIV infection

Children < 18 months:

- **Birth:** Do an HIV PCR at birth in all HIV-exposed infants.

» **10 Weeks:** Do an HIV PCR at 10 weeks of age (chronological age) in all HIV-exposed infants.
» **6 Months:** Do an HIV PCR at 6 months of age in all HIV-exposed infants.
» The HIV status of all children not already known to be HIV-exposed should be established by offering the mother an HIV test at any time point.
» **Post cessation of breastfeeding:** If the child is breastfed and previous HIV PCRs were negative, repeat testing 6 weeks after complete cessation of breastfeeding. (If the child is 18 months or older, do an HIV ELISA or rapid test).
» **Suspected symptomatic HIV infection:** If the child has evidence suggesting HIV infection at any time, even if the child has had a previous negative HIV PCR test, the child should be tested for HIV infection.
» If the HIV PCR is positive at any time point:
  > Confirm with a repeat HIV PCR test.
  > Initiate treatment while awaiting the second HIV PCR test result.

Children ≥ 18 months:

» **18 months:** Universal HIV testing at 18 months (HIV rapid test for ALL infants regardless of HIV exposure, except in those who previously tested HIV-positive and are on ART).
» **Suspected symptomatic HIV, possible HIV, HIV unknown or Ongoing HIV exposure:** Do an HIV rapid or ELISA test.
» If the first rapid test is positive, confirm the result with:
  > An HIV PCR test if the infant is between 18–24 months.
  > A second rapid test using a different manufacturer kit, preferably on a different blood specimen, if the infant is > 24 months.

Note:
Rapid tests may be less reliable in children with advanced disease. If clinical findings suggest HIV infection, but the rapid test is negative, send a further specimen of blood to the laboratory for formal HIV ELISA testing. If test results are still equivocal, do an HIV PCR test.

Note:

» A child cannot be confirmed as HIV-negative until at least 4–6 weeks after other potential HIV exposure (including cessation of breastfeeding). Exposure to ART through prophylaxis (NVP/AZT) or maternal ART may affect the sensitivity of HIV PCR tests.
» Manage children with discordant or indeterminate HIV test results as per the National Department of Health Guidelines for the Prevention of Mother to Child Transmission of Communicable Infections (HIV, Hepatitis, Listeriosis, Malaria, Syphilis and TB).

9.1.1 THE HIV-EXPOSED INFANT

Z20.6

DESCRIPTION

Infants and children born to mothers living with HIV until HIV infection in the infant or child is reliably excluded and the infant or child is no longer exposed through breastfeeding are defined as HIV-exposed.

Transmission of HIV infection may occur during pregnancy, during delivery, or via breastfeeding. Vertical transmission prevention (VTP) can be effectively carried out with a very high success rate by fully suppressing the mother's viral load with ART and giving prophylactic antiretroviral therapy to the infant. Maternal viral loads must be done, checked, recorded and acted upon during pregnancy and breastfeeding. The risk of breast milk transmission remains significant when the mother's viral load cannot be suppressed.

The VTP strategies include the initiation of ART in the mother (either pre- or post-conception) and the provision of HIV post-exposure prophylaxis to the infant. The mother's response to ART by the time of delivery is measured by the delivery VL. The delivery VL will determine the risk profile of the infant at birth. The risk profile of the infant (low-risk or high-risk) will determine the appropriate infant prophylaxis regimen that should be prescribed. All HIV-exposed infants will be considered high-risk until the results of the delivery viral load are known. Therefore, if the delivery VL result is not available at the time of discharge, the HIV-exposed infant will be considered high-risk until the result can be reviewed at the 3–6 day postnatal visit.

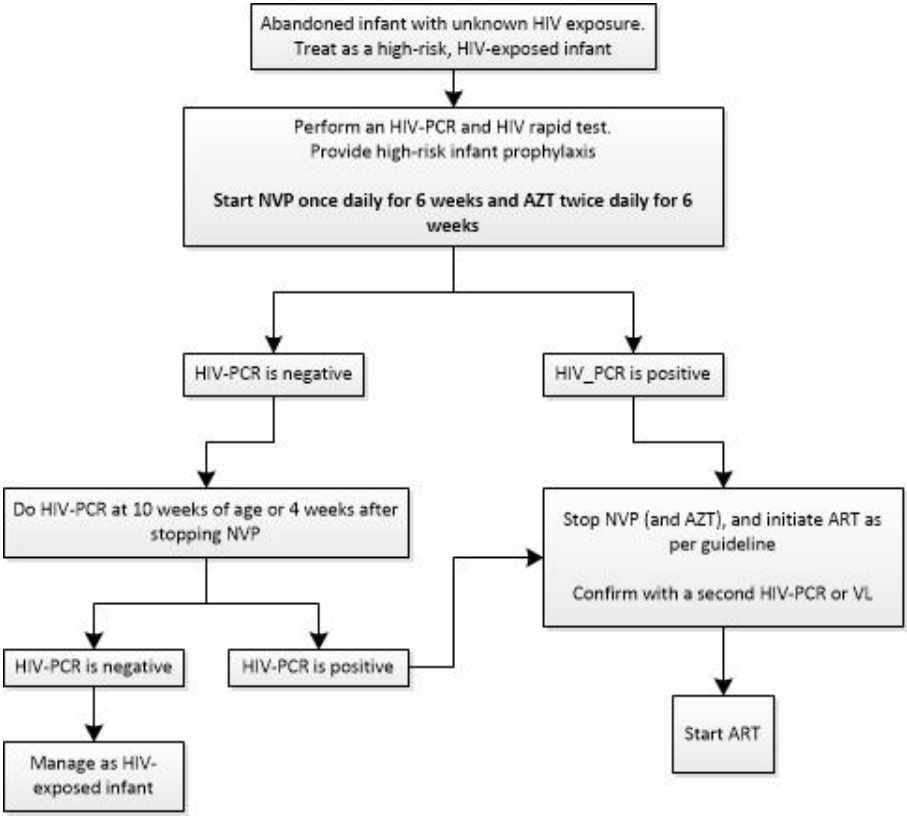
MANAGEMENT OF HIV-EXPOSED INFANTS

Maternal VL	Risk profile	Prophylaxis	Comment
Maternal delivery VL as yet unknown at discharge from labour ward (results pending).	High-risk (until maternal delivery VL results become available)	Provide dual prophylaxis: AZT at birth and then twice daily for 6 weeks. NVP at birth and then daily for a minimum of 12 weeks.	All HIV-exposed infants will be considered high-risk until the final risk profile can be determined by the maternal delivery VL. If the maternal delivery VL result is not available at discharge from labour ward, review result at the 3–6 day postnatal visit and reclassify the infant accordingly.

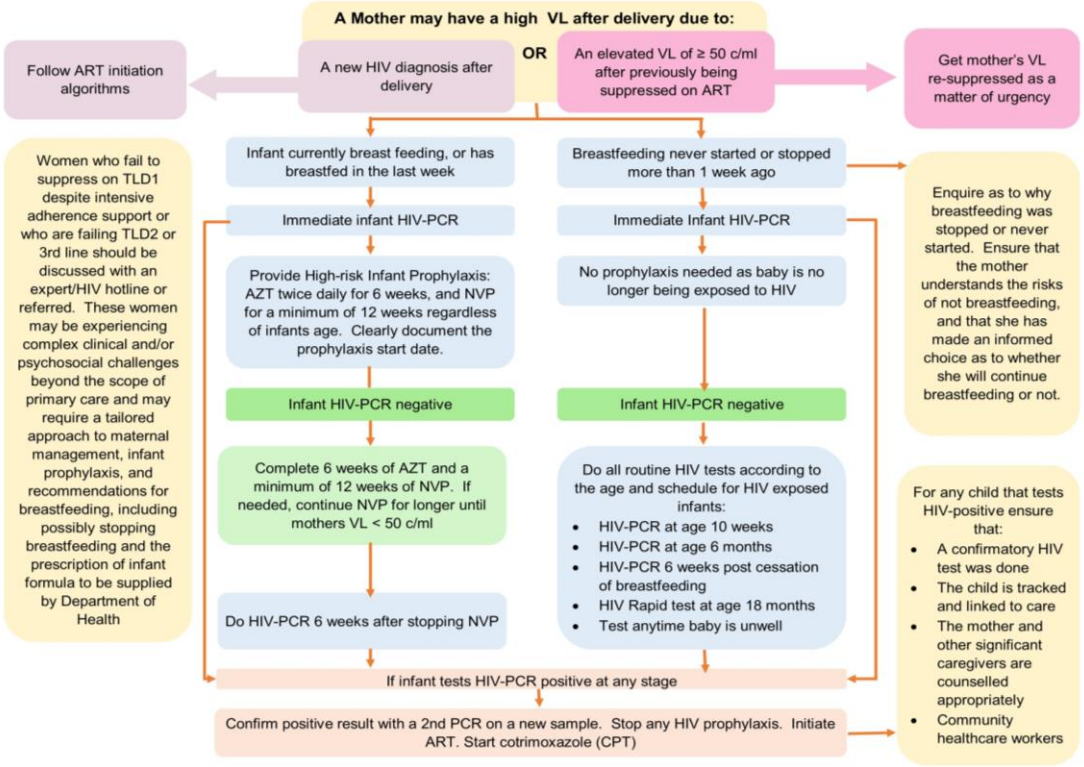
Maternal VL	Risk profile	Prophylaxis	Comment
			Dispense a full 6 weeks supply of dual prophylaxis. Ask the mother to return with all medication at the 3–6 day postnatal visit.
Maternal delivery VL ≥ 50 copies/mL in a breastfeeding mother.	High-risk	Provide dual prophylaxis: AZT at birth and then twice daily for 6 weeks. NVP at birth and then daily for a minimum of 12 weeks.	Do an ABCDE assessment and get the mother's VL re-suppressed as a matter of urgency. Stop infant NVP only after confirmation of maternal VL being < 50 copies/mL, or until 4 weeks after cessation of all breastfeeding.
Maternal delivery VL ≥ 50 copies/mL in a mother who is exclusively formula feeding her infant from birth.*	High-risk	Provide dual prophylaxis: AZT at birth and then twice daily for 6 weeks. NVP at birth and then daily for 6 weeks.	Do an ABCDE assessment and get the mother's VL re-suppressed as a matter of urgency.
Maternal delivery VL < 50 copies/mL regardless of feeding choice.	Re-classify as low-risk.	Change to low-risk prophylaxis: NVP at birth and then daily for 6 weeks.	Affirm and encourage good adherence. Repeat maternal VL 6-monthly during breastfeeding.

***Non-breastfeeding mother diagnosed HIV-positive > 72 hours after delivery:** *Do not start the infant on prophylaxis. Start maternal ART. Perform an HIV PCR test on the infant and, if positive, initiate ART, if negative, continue to monitor HIV risk and perform HIV testing as above.*

Unknown maternal status



Management of high maternal viral load after delivery



Nevirapine (NVP) and Zidovudine (AZT) doses for an infant on PMTCT

- Nevirapine, oral, daily (syrup 10 mg/mL) and zidovudine, oral, twice daily (syrup 10 mg/mL).
    - Newborns ≥ 2 kg and term infants:

	Birth–6 weeks		***6 weeks–6 months***	***6–9 months***	***9–24 months***
	2.0–2.49 kg	≥ 2.5 kg			
NVP (Daily)	1 mL (10 mg) daily	1.5 mL (15 mg) daily	2 mL (20 mg) daily	3 mL (30 mg) daily	4 mL (40 mg) daily
AZT (Twice daily)	1 mL (10 mg) twice daily	1.5 mL (15 mg) twice daily	6 mL (60 mg) twice daily	Children > 6 months of age requiring AZT prophylaxis should use treatment doses.	

LoE I[2]

    - Preterm newborn < 2 kg:
        - Nevirapine, oral, daily:

Weight	**First 2 weeks after birth (mg of NVP)**	**After first 2 weeks after birth (mg of NVP)**
500 to < 625 g	1 mg	2 mg
625 to < 850 g	1.5 mg	3 mg
850 to < 1200 g	2 mg	4 mg
1.2 to < 1.5 kg	3 mg	5 mg
1.5 to < 2 kg	3.5 mg	6 mg
If the infant at the time of discharge is severely underweight-for-age (3 SD or 3 z-scores below the mean), give NVP according to weight (i.e. 4 mg/kg/dose daily) until in the normal weight-for-age range.		

        - Zidovudine, oral, twice daily:

Gestational age at birth	**First 2 weeks after birth**	**2–4 weeks after birth**	**4–6 weeks after birth**	**> 6 weeks after birth**
30–35 weeks	2 mg/kg	3 mg/kg	4 mg/kg	
< 30 weeks	2 mg/kg		3 mg/kg	4 mg/kg

LoE II[3,4,5]

See table above.

» Ideally, the birth HIV PCR test should be done before administration of infant NVP and AZT, but any delay in testing should not delay administration.

» Repeat the dose if the baby vomits.

» If the infant's HIV PCR is positive at any time, stop NVP and AZT, perform a second HIV PCR test and initiate ART immediately. Counsel the mother to continue breastfeeding.

ART Prophylaxis for infants who are unable to tolerate oral medication

Infants who are unable to tolerate oral medication/feeds should be initiated on intravenous zidovudine (AZT). On re-establishment of oral feeds/ medications, intravenous zidovudine should be stopped, and the infant should commence on the appropriate oral infant prophylaxis regimen. Ideally, gestational age should be used to determine the optimal dose.

Gestational Age	Approximate birth weight	AZT IV dosing for the first 14 days (If unable to tolerate oral agents)
≥ 35 weeks	≥ 2.5 kg	3 mg/kg body weight, IV every 12 hours
< 35 weeks	< 2.5 kg	1.5 mg/kg body weight, IV every12 hours

HIV TESTING

Age appropriate testing

» < 18 months – do an HIV PCR.
» ≥ 18 months – do a rapid HIV antibody test or ELISA.
  > Confirm the HIV test in children between 18–24 months with an HIV PCR.
  > Confirm the HIV test in children > 24 months with an HIV rapid test.

Routine testing for HIV-exposed children < 18 months:

» **Birth:** Do an HIV PCR at birth in all HIV-exposed infants.
» **10 Weeks:** Do an HIV PCR at 10 weeks of age (chronological age) in all HIV-exposed infants.
» **6 Months:** Do an HIV PCR at 6 months of age in all HIV-exposed infants.
» The HIV status of all children not already known to be HIV-exposed should be established by offering the mother an HIV test at any time point.
» **Post cessation of breastfeeding:** If the child is breastfed and previous HIV PCRs were negative, repeat testing 6 weeks after complete cessation of breastfeeding. (If the child is 18 months or older, do an HIV ELISA or rapid test).

Routine testing for all children ≥ 18 months:

» **18 months:** Universal HIV testing at 18 months (HIV rapid test for ALL infants regardless of HIV exposure, except in those who previously tested HIV-positive and are on ART).
» If the first rapid test is positive, confirm the result with:
  > An HIV PCR test if the infant is between 18–24 months.
  > A second rapid test using a different manufacturer kit, preferably on a different blood specimen, if the infant is > 24 months.

Testing for all children regardless of age or HIV-exposure status:

» **Symptomatic child/infant:** If the child has evidence suggesting HIV infection at any time, even if the child has had a previous negative HIV PCR test, the child should be tested for HIV infection using an age-appropriate HIV test (HIV PCR or rapid test).
» If the HIV test is positive at any time point:
  > Confirm with a repeat age-appropriate HIV test.
  > Initiate treatment while awaiting the second HIV test result.

Note:

» Repeat HIV PCR testing at 10 weeks and 6 months should be done on all HIV-exposed infants with a prior negative or indeterminate HIV PCR.
» Any infant with a positive birth HIV PCR should be urgently initiated on ART as per section 9.1.2: The HIV-Infected neonate.
» A child cannot be confirmed as HIV-negative until at least 4–6 weeks after other potential HIV exposure (including cessation of breastfeeding). Exposure to ART through prophylaxis (NVP/AZT) or maternal ART may affect the sensitivity of HIV PCR tests.
» Rapid tests may be less reliable in children with advanced disease. If clinical findings suggest HIV infection, but the rapid test is negative, send a further blood specimen to the laboratory for formal HIV ELISA testing. If test results are still equivocal, do an HIV PCR test.
» Patients already on ART should not have a repeat HIV antibody (rapid) test.

If an HIV PCR test is indeterminate or discordant, refer to the National Department of Health Guidelines for prevention of Mother to Child Transmission of Communicable Infections. 2023.

All HIV PCR results need to be followed-up as a matter of urgency.

Feeding advice

» It is strongly recommended that exclusive breastfeeding be initiated within 1 hour of birth and continued for the first 6 months of life, after which the child's nutritional requirements will require the introduction of complementary foods in addition to breastfeeding.
» Women living with HIV should be fully supported for ART adherence during the breastfeeding period and thereafter.
» Women with a VL > 50 copies/mL on TLD1 should continue breastfeeding while every effort is made to regain viral suppression. Their infants should receive high-risk prophylaxis during breastfeeding.
» The following may be indications to discontinue breastfeeding:
  > Infants of mothers who are failing TLD2.
  > Infants of mothers who are failing third-line PI-based treatment.
» Discuss appropriate feeding practices with the mother regarding the risks and benefits of continuing breastfeeding vs replacement feeding.

» The use of flash pasteurisation or 'Pretoria' pasteurisation to reduce HIV transmission is supported but may pose significant barriers to successful breast milk feeding due to the effort involved. For instance, it can be used as an interim measure during maternal mastitis.

Cotrimoxazole prophylaxis

Indications:

» According to the current guideline, only babies with a positive HIV PCR should be started or continued on cotrimoxazole prophylaxis as per section 9.1.2: The HIV-Infected neonate, medicine treatment, cotrimoxazole prophylaxis below.

9.1.2 THE HIV-INFECTED NEONATE (< 1 MONTH OF AGE)

B20-B24

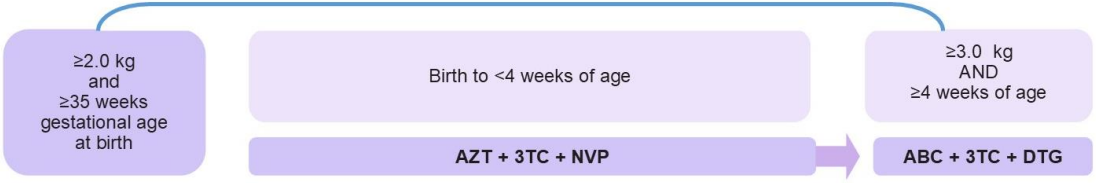
DESCRIPTION

Defined as an infant < 1 month of age, in whom HIV infection has been confirmed with two appropriate tests. For confirmation of HIV infection, see section 9.1: Human immunodeficiency virus infections.

MEDICINE TREATMENT

This treatment protocol is meant as a guide, and there is an allowance for flexibility after discussion with an expert.

Protocol for initiation of ART at < 4 weeks of age: HIV-infected neonates ≥ 2.0 kg & 35 weeks gestational age at birth



Baseline Assessment

- Clinical review
- Bloods: confirmatory HIV PCR (or HIV VL), CD4 count, FBC +/- HIV drug resistance test if mother failing treatment on TLD2 or a protease inhibitor regimen
- Counsel parent / caregiver
- Ensure mother on ART / advise on breastfeeding

Review after 1 week then 1-2 weekly

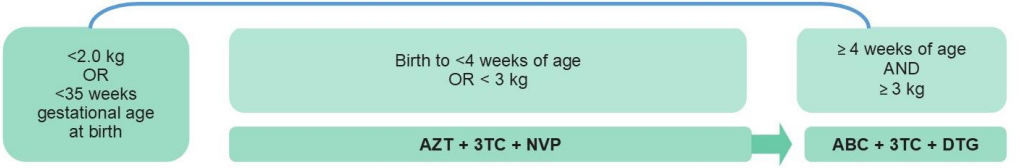
- Clinical review and counselling
- Check baseline blood results
- If indeterminate / negative confirmatory HIV PCR test result, refer to Guideline for Family-Centered Transmission Prevention of Communicable Infections

Review when 4 weeks of age

- Clinical review and counselling
- If <3 kg, assess reasons for poor weight gain & manage appropriately, continue ART with AZT (12 mg/kg/dose twice daily) + 3TC (4 mg/kg/ dose twice daily) + NVP (6 mg/kg/dose twice daily) until ≥3.0 kg
- If >3 kg, switch ART to ABC + 3TC + DTG (refer to ARV dosing chart for doses)
- Continue monitoring and evaluations as per section 9.1.3 of Paediatric Hospital Level EML

	Zidovudine (AZT)		Lamivudine (3TC)		Nevirapine (NVP)	
Available formulation	Solution 10 mg/mL		Solution 10 mg/mL		Solution 10 mg/mL	
Weight (kg) at birth	Dose		Dose		Dose	
	AM	PM	AM	PM	AM	PM
≥2.0 – <3.0	10 mg (1 mL)	10 mg (1 mL)	5 mg (0.5 mL)	5 mg (0.5 mL)	15 mg (1.5 mL)	15 mg (1.5 mL)
≥3.0 – <4.0	15 mg (1.5 mL)	15 mg (1.5 mL)	8 mg (0.8 mL)	8 mg (0.8 mL)	20 mg (2 mL)	20 mg (2 mL)
≥4.0 – <5.0	20 mg (2 mL)	20 mg (2 mL)	10 mg (1 mL)	10 mg (1 mL)	30 mg (3 mL)	30 mg (3 mL)

Protocol for initiation of ART at < 4 weeks of age: HIV-infected preterm infants < 2 kg & 35 weeks gestational age at birth



Baseline Assessment

- Clinical review
- Bloods: confirmatory HIV PCR (or HIV VL), CD4 count, FBC +/- HIV drug resistance test if mother failing treatment on TLD2 or a protease inhibitor regimen
- Counsel parent / caregiver
- Ensure mother on ART / advise breastfeeding recommended for all positive infants.

Review after 1 week then 1-2 weekly

- Clinical review an counselling
- Check baseline blood results
- If indeterminate / negative confirmatory HIV PCR test result, refer to Guideline for Family-Centered Transmission Prevention of Communicable Infections
- Monitor weight gain and adjust ARV doses

Review when ≥4 weeks of age

- Clinical review and counselling
- If <3 kg, continue AZT + 3TC + NVP
- If >3 kg, switch to ABC + 3TC + DTG (refer to ARV dosing chart for doses)
- Continue monitoring and evaluations

Gestational age at birth	Chronological age	Zidovudine (AZT)	Lamivudine (3TC)	Nevirapine (NVP)
		Solution 10 mg/mL	Solution 10 mg/mL	Solution 10 mg/mL
<30 weeks	Birth to < 4 weeks	2 mg/kg/dose twice daily	2 mg/kg/dose twice daily	2 mg/kg/dose twice daily
	> 4 weeks to < 8 weeks	3 mg/kg/dose twice daily	4 mg/kg/dose twice daily	4 mg/kg/dose twice daily
	> 8 weeks to < 10 weeks	12 mg/kg/dose twice daily		6 mg/kg/dose twice daily
≥ 30 to < 35 weeks	Birth to < 2 weeks	2 mg/kg/dose twice daily	2 mg/kg/dose twice daily	2 mg/kg/dose twice daily
	> 2 to <4 weeks	3 mg/kg/dose twice daily		4 mg/kg/dose twice daily
	> 4 to <6 weeks		4 mg/kg/dose twice daily	6 mg/kg/dose twice daily
	> 6 to < 8 weeks	12 mg/kg/dose twice daily		

Caregivers administering ARV medication to the child must be supplied with a syringe (1 mL or 2 mL) for each of the three ARVs and shown how to prepare and administer the correct dose. If possible, bottles and syringes should be colour-coded with stickers, and a sticker of the relevant colour should be used to mark the correct dose on the syringe.

LoE III[6]

9.1.3 THE HIV-INFECTED INFANT/CHILD (< 10 YEARS)

B20-24

DESCRIPTION

Defined as an infant or child in whom HIV infection has been confirmed with two appropriate tests.

For confirmation of HIV infection, see section 9.1: Human immunodeficiency virus infections.

GENERAL AND SUPPORTIVE MEASURES

Counselling is a vital part of the successful care of children with HIV infection and their families. Specific matters requiring attention are:

» The implications of the disease to the family.
» Implications of treatment, non-adherence and understanding of the condition and its care.
» The disclosure process within the family and extended family/friends should be encouraged. Help from family/friends is often useful.
» Disclosure to the child of appropriate age and maturity.

Treatment of mothers, caregivers and other family members:

» Always ask about the caregiver's health and the health of other members of the family.
» Ensure that mothers and other family members have timeous access to medical care, including ART.
» Encourage breastfeeding in all mothers with HIV-infected children, with the introduction of weaning foods from 6 months of age. Breastfeeding duration is recommended for 2 years or longer, as in HIV-unexposed children.
» Always ask, at every visit, about TB contacts and TB symptoms in all children and their caregivers.

STANDARDISED NATIONAL MONITORING FOR INFANTS AND CHILDREN WITH HIV

At initial diagnosis of HIV	Purpose
Confirm HIV status.	To ensure that the national testing algorithm has been followed.
Document weight, height, head circumference (HC if < 2 years of age) and development.	To monitor growth and development.
Screen for TB symptoms.	To identify TB co-infection.
Do CD4 count.	To determine eligibility for cotrimoxazole prophylaxis (CPT): < 1 year: CPT irrespective of CD4 count. 1–5 years: CPT if CD4 count < 25% or WHO Stage 2–4. > 5 Years: CPT if CD4 count < 200 cells/mm^3 or WHO Stage 2–4.
At the initiation of ART (baseline)	**Purpose**
Hb or FBC.	If < 8 g/dL, manage appropriately.
CD4 count (if not performed in the last 6 months).	Baseline assessment.
ALT (if jaundiced or on TB treatment).	To assess for liver dysfunction at baseline.
On ART	**Purpose**
Height, weight, head circumference (HC if < 2 years of age) and development.	To monitor growth and development stages. Adjust dosing at each visit as necessary according to weight gain.
Clinical assessment, including drug-related adverse events.	To monitor response to ART and exclude adverse effects.
CD4 count: At 1 year on ART, and then every 6 months until they meet the criteria to stop cotrimoxazole. Thereafter, stop CD4 count monitoring if the patient remains virologically suppressed.	To monitor response to ART and stop cotrimoxazole prophylaxis as indicated.

If not virologically suppressed, monitor CD4 count every 6 months.	
Viral load (VL): At month 3 on ART, after 12 months on ART, then every 12 months if virologically suppressed. More frequent monitoring (3–6 monthly) recommended in patients with treatment failure.	To monitor viral suppression on ART. To identify treatment failure and identify adherence problems.
If on AZT, Hb or FBC and differential WBC at months 3 and 6. Thereafter, repeat if clinically indicated.	To identify AZT-related anaemia.
If on a PI, cholesterol + triglyceride at month 3. If above the acceptable range, do fasting cholesterol and TGs, and obtain expert advice if still above the acceptable range.	To monitor for PI-related metabolic side effects.

MEDICINE TREATMENT

Cotrimoxazole prophylaxis

Indications:

» According to the current guideline, babies with a positive HIV PCR should be started and continued on cotrimoxazole prophylaxis until criteria for discontinuation are met.

- Cotrimoxazole (sulfamethoxazole/trimethoprim), oral, once daily (every day).

Recommended daily dosage by weight band	Dose of sulfa-methoxazole/ trimethoprim	Suspension (200/40 mg per 5 mL)	Single strength tablet (400/80 mg)	Double strength tablet (800/160 mg)
3 to 5.9 kg	100/20 mg	2.5 mL	¼ tablet	–
6 to 13.9 kg	200/40 mg	5 mL	½ tablet	–
14 to 24.9 kg	400/80 mg	10 mL	1 tablet	½ tablet
25 kg	800/160 mg	–	2 tablets	1 tablet

Discontinuation:

» If HIV-infected, the immune system is fully reconstituted on ART and child > 1 year of age (i.e. child 1 to 5 years of age: CD4 > 25% or child > 5 years of age: CD4 > 200 cells/mm^3 on two tests at least 3–6 months apart).

Immunisation, deworming and vitamin A program

» Continue deworming and vitamin A programme as in the HIV-negative child.

» Continue immunisation as in the HIV-negative child. See the Standard Treatment Guidelines and Essential Medicines List for Primary Health Care, Chapter 13: Immunisation.

Nutritional support

Specific nutritional conditions should be treated appropriately.

Antiretroviral therapy (ART)

Initiation of ART in clinically stable HIV-infected children without complications should be at PHC level – see national NIMART guidelines (IMCI) and Standard Treatment Guidelines and Essential Medicines List for Primary Health Care.

Preparing the child and family to start ART is critical to the success of the treatment. Failure to achieve adherence may lead to resistance and adversely affect the child's prognosis.

Eligibility criteria for antiretroviral therapy

» Confirmation of diagnosis of HIV infection irrespective of CD4 count or WHO clinical staging.

AND

» No medical contraindication (e.g. major organ dysfunction). If medical contraindications are present, refer to the hospital for rapid review and planning.

Social issues that must be addressed to ensure successful treatment

These are extremely important for success as they impact adherence.

Social challenges should be continuously addressed and not be barriers to access to care.

Disclosure to another adult living in the same house is encouraged so that someone else can assist with the child's treatment.

» Mandatory component: at least one identifiable caregiver can supervise the child and/or administer medication. All efforts should be made to ensure that the social circumstances of vulnerable children, e.g. orphans, be addressed to facilitate treatment.

» Adherence:
  > High levels of adherence should be maintained for adequate virological response and prevention of viral resistance. This can be achieved with regular education and support.
  > All efforts to encourage this level of adherence should be made.
  > Viral load measurements are useful for monitoring adherence.

» Sensitive, age-appropriate disclosure facilitates adherence.

Requirements before ART is used

The child's family (parents, caregivers) should understand:

» that antiretroviral therapy is long-term,
» the prognosis of the condition (treated and untreated),
» adverse effects of the medicines, their mode of action, and the risk and implications of developing resistance, if incorrectly used,
» that all medications should be given as prescribed and adequately stored.

ART Regimens

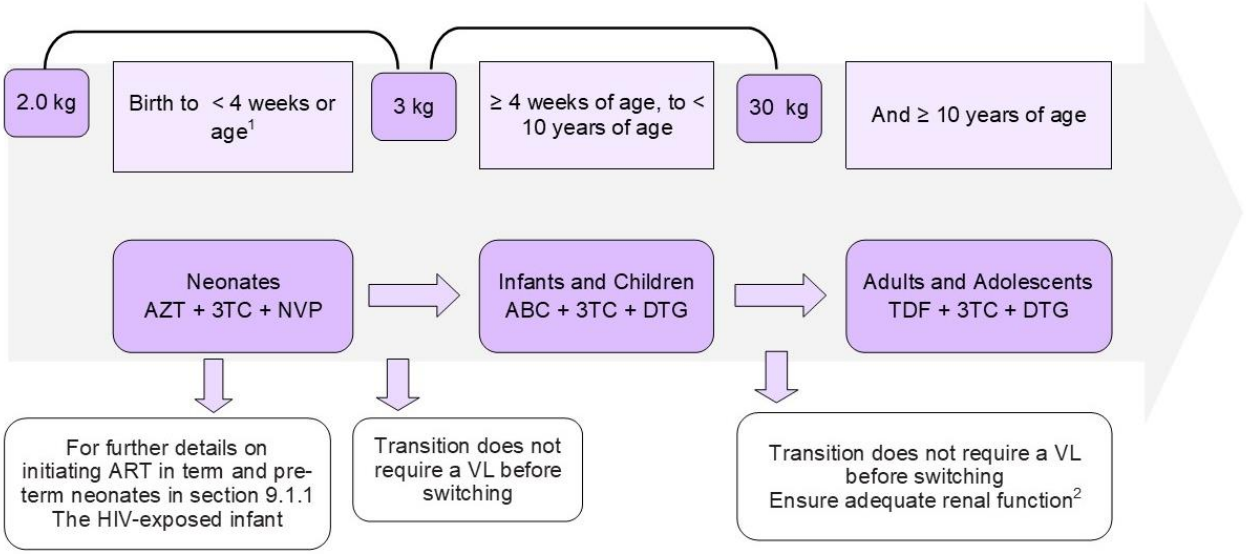
» These are chosen according to age, weight, expected adverse effects, efficacy, and prior antiretroviral exposure.
» Adjust the dosage of antiretroviral therapy according to weight during follow-up visits. Assess weight gain and need for adjustment at each visit.
» Do not change regimens or move to second-line therapy without clear guidance from an experienced practitioner in child ARV medicine. An unnecessary loss of effective regimens can shorten life expectancy. Adherence problems need to be addressed thoroughly when switching to a second- or third-line regimen.
» Single drug substitution should be discussed with an experienced practitioner in child ARV medicine.

TLD1: Clients on a DTG-containing regimen, having never failed a previous regimen (old 'first-line' terminology).

TLD2: Clients on a DTG-containing regimen, who have failed a previous regimen (old 'second- line' terminology).

TLD: tenofovir, lamivudine, dolutegravir.

Recommended regimen in ART-naïve Neonates, Infants, Children 0 to < 10 years of age



1. For neonates with severe anaemia, obtain advice from an expert or through one of the helplines
2. Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine

Switching existing clients to DTG-containing regimens

Non VL-dependent regimen switches Regimens where the VL result will not influence nor delay the decision to switch to DTG-containing regimen			
VL considerations	**Current Regimen**	**Criteria for switch**	**Regimen if change indicated**
Switching regardless of VL result	**TEE** **ABC/3TC/EFV** **AZT/3TC/EFV** **AZT/3TC/DTG** **Any LPV/r or ATV/r regimen for less than 2 years**	**Switch all to a DTG-containing regimen, regardless of VL result** Review VL in last 12 months. If VL in last 12 months was not suppressed, continue to switch same day, but do ABCDE assessment and provide enhanced adherence counselling (EAC) if needed. If VL was not done in last 12 months, do it at this visit, but do not wait for results to switch.	**TLD** Provided no renal dysfunction and age > 10 years and weight > 30 kg If client does not quality for TDF **ABC[1]/3TC/DTG** If client does not quality for TDF and has ABC hypersensitivity **AZT/3TC/DTG**

VL-dependent regimen switches Relevant to all clients who have been on PI-based regimens for more than two years: their VL result in the last 12 months will influence the decision of how and when to switch to a DTG-containing regimen			
VL considerations	**Current Regimen**	**Criteria for switch**	**Regimen if change indicated**
VL < 1000 c/mL	**Any LPV/r or ATV/r regimen for more than 2 years**	**Switch all to a DTG-containing regimen** If VL in last 12 months was not < 50 c/mL, continue to switch same day, but do ABCDE assessment and provide EAC if needed.	**TLD** provided no renal dysfunction and age > 10 years and weight > 30 kg If clients does not qualify for TDF **ABC[1]/3TC/DTG**
[2] Two or more VLs ≥ 1000 c/mL taken two or more years after starting PI regimen	Adult or adolescent on any **LPV/r or ATV/r** regimen and adherence **less than 80%[3]**	**Switch all to a DTG-containing regimen** **Do not do a resistance test** These clients are unlikely to have PI resistance mutations. Rather switch to a more tolerable once daily FDC regimen which is likely to support adherence.	**TLD** provided no renal dysfunction and age > 10 yrs and weight > 30 kg If clients does not qualify for TDF **ABC[1]/3TC/DTG**
	Adult or adolescent on any **LPV/r or ATV/r regimen and adherence more than 80%[3]**	Clients who meet the definition of confirmed virological failure despite confirmed adherence more than 80% may need a resistance test. **These clients do not qualify for a same-day switch**. Discuss with an HIV expert[4] to authorise and interpret a resistance test. Provide individualised regimen as recommended by HIV expert.	
	Child < 10 years, or weight < 30 kg on any **LPV/r or ATV/r regimen**	These clients do not yet qualify for TLD and may require a resistance test. Refer to algorithm "**Switching children on PI-containing regimens to DTG-containing regimens**"	

1. If clients are not eligible to use TDF and they have ABC hypersensitivity, use AZT/3TC/DTG.
2. Confirmed virological failure is defined as two or more VLs ≥ 1000 c/mL taken two or more years after starting a DTG or PI containing regimen, despite adherence > 80% by objective measurement. A patient who has only 1 VL > 1000 after 2 years on a PI-based regimen should have an ABCDE assessment, EAC if applicable, and their VL repeated in 3 months. The result of the repeat VL will allow the patient to be grouped into one of the categories in the table above and will inform the further course of action.
3. Objective measures of good adherence include at least one of:
   - Pharmacy refills > 80% in the last 6-12 months (if this is known).
   - Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known).
   - Detection of current antiretroviral drug/s in the client's blood or urine, if available.

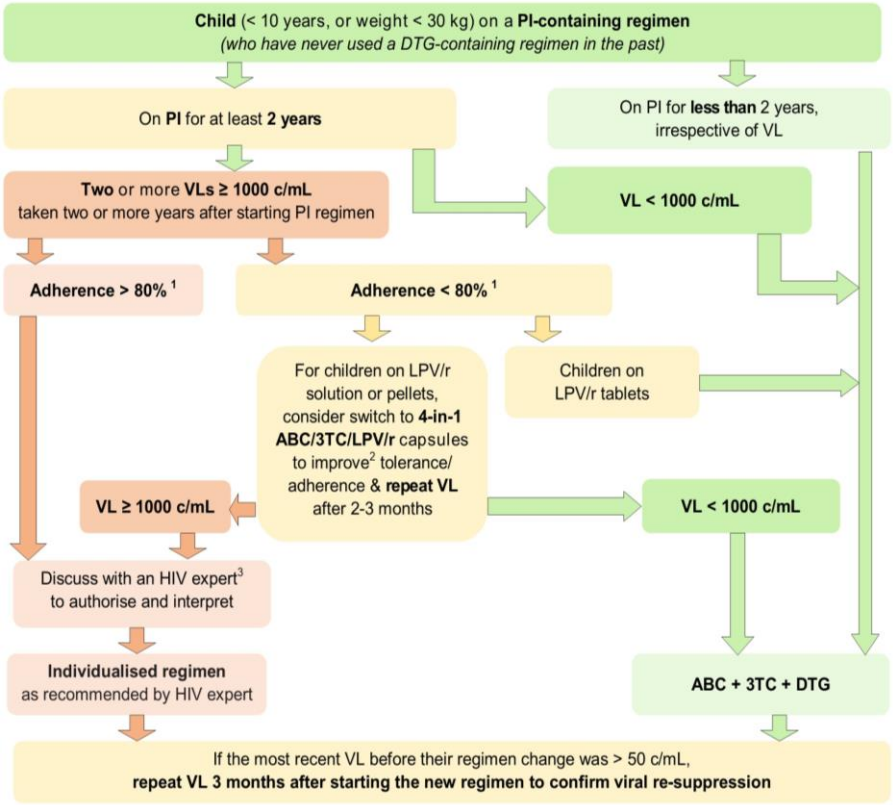
   Note: Self-reported adherence is not considered a reliable measure of good adherence.
4. For advice from an HIV expert, approach an HIV Hotline, an infectious disease specialist, or the Third Line ART committee.

Transition from ABC/3TC/LPV/r to DTG based regimens

ALL children < 10 years and < 30 kg on ABC/3TC/LPV/r switch to ABC/3TC/DTG.
EXCEPT if VL > 1000 copies/mL (performed in the last 12 months) for > 2 years.

- Consider switching to ABC/3TC/LPV/r 4-in-1 formulation and repeating HIV VL in 3 months. If HIV VL < 1000 copies/mL, change to ABC/3TC/DTG and if > 1000 copies/mL, perform an HIV drug resistance test (DR)
- Perform an HIV DR if 4-in-1 formulation not available.
- If NRTI mutations on the HIV DR show:
    - No mutations or only M184V – switch to ABC/3TC/DTG.
    - M184V + other mutations – discuss with an experienced practitioner in child ARV medicine.

Switching children on PI-containing regimens to DTG regimens



1. Although objective measures of poor adherence include pharmacy refills or attendance of scheduled clinic visits in the previous 6-12 months of <80%, adherence difficulties in young children are often linked to poor tolerability of unpalatable formulations, particularly LPV/r solution. It is important to ask the caregiver about how the child tolerates the medication e.g., does the child refuse to swallow the medicine or spit out or vomit the medicine, and whether the caregiver has been able to overcome this. Considering these limitations, objective measures of good adherence could include one of the following:
    a. Pharmacy refills > 80% in the last 6-12 months (if this is known)
    b. Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
    c. Detection of current antiretroviral drug/s in the client's blood or urine, if available
2. If a switch to the 4-in1 capsules does not improve adherence, or is not available, continue to switch to ABC + 3TC + DTG as for non-adherent children on LPV/r tablets.
3. The following would qualify as HIV experts: the HIV Helplines, a paediatric infectious disease specialist or the paediatric Third line ART committee .

Treatment failure

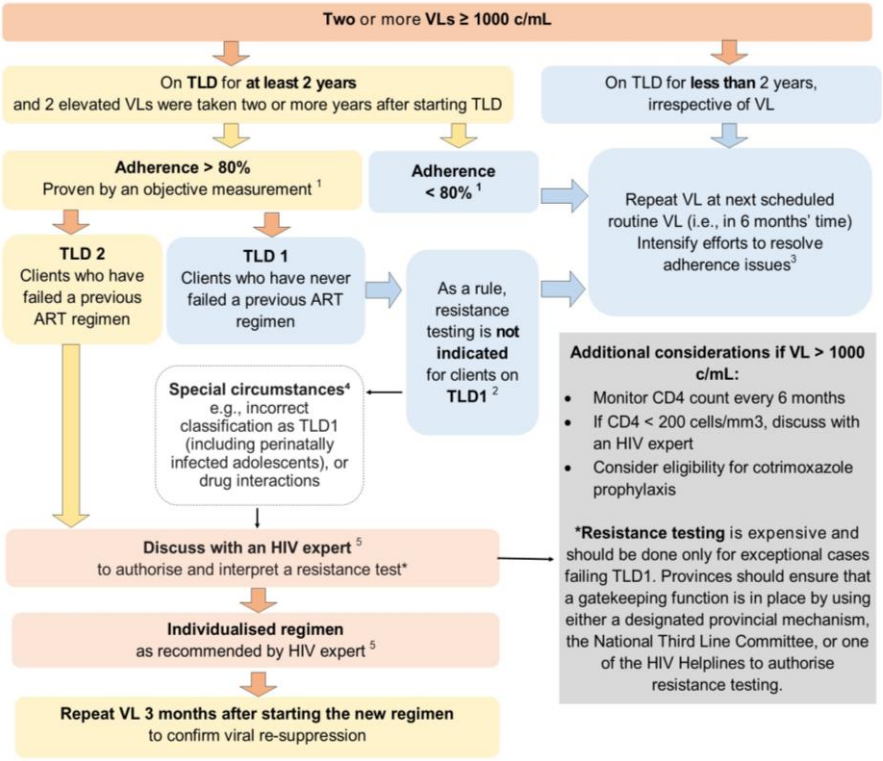
The HIV viral load is the most sensitive method to detect failure of response to ART.

Virological failure can be defined as a measurable viral load despite optimal adherence and dosage over 4 months. Treatment failure is primarily defined by viral loads, as waiting for clinical or immunological failure increases the chances of increasing viral resistance to other available antiretroviral agents.

Poor adherence is the most common cause of treatment failure. Adherence issues should be assessed and then implement strategies to improve adherence.

*For guidance on the step-up adherence package, refer to the National adherence guidelines.
https://www.nacosa.org.za/wp-content/uploads/2016/11/Integrated-Adherence-Guidelines-NDOH.pdf

Management of confirmed virological failure in adolescents on TLD



1. Objective measures of good adherence include at least one of:
   - Pharmacy refills > 80% in the last 6-12 months (if this is known)
   - Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   - Detection of current antiretroviral drug/s in the client's blood or urine, if available

   Note: Self-reported adherence is not considered a measure of good adherence!
2. Due to their high genetic barrier, resistance to a first-line DTG-containing regimen (TLD1) is extremely rare. If other reasons for an unsuppressed VL have been addressed or excluded, e.g., drug interactions and the client remains unsuppressed at their repeat VL, suboptimal adherence remains the most probable cause for non-suppression. The highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. 99,9% of these clients will re-suppress on TLD if adherent.
3. Repeat the ABCDE assessment. Remember to ask about treatment side-effects, the potential cost of transport or loss of income related to clinic visits, mental health conditions, non-disclosure, poor social support, or substance abuse. If necessary, discuss with an expert or refer to other multidisciplinary team members, if available.
4. Special circumstances that may warrant a resistance test for clients on TLD1 include:
   - Incorrect classification as TLD1 (clients who declare themselves as never having had ART before, but who have actually been exposed to ART and may have failed a regimen in the past).
   - Perinatally infected adolescents: Unless a clearly documented drug history is available, perinatally infected adolescents should be classified as TLD2 due to the high likelihood of ART exposure and virological failure in the past.
   - Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen.

   In these types of exceptional circumstances, TLD1 clients with persistent virological failure despite confirmed good adherence may be discussed with an expert to authorise a resistance test on a case-by-case basis.
5. For advice from an HIV expert, approach an HIV Hotline, an infectious disease specialist, or the Third Line ART committee.

Third-line

Application forms for third-line antiretroviral therapy can be accessed at the following link:

Application for Third Line Antiretrovirals_2017.pdf (sahivsoc.org)

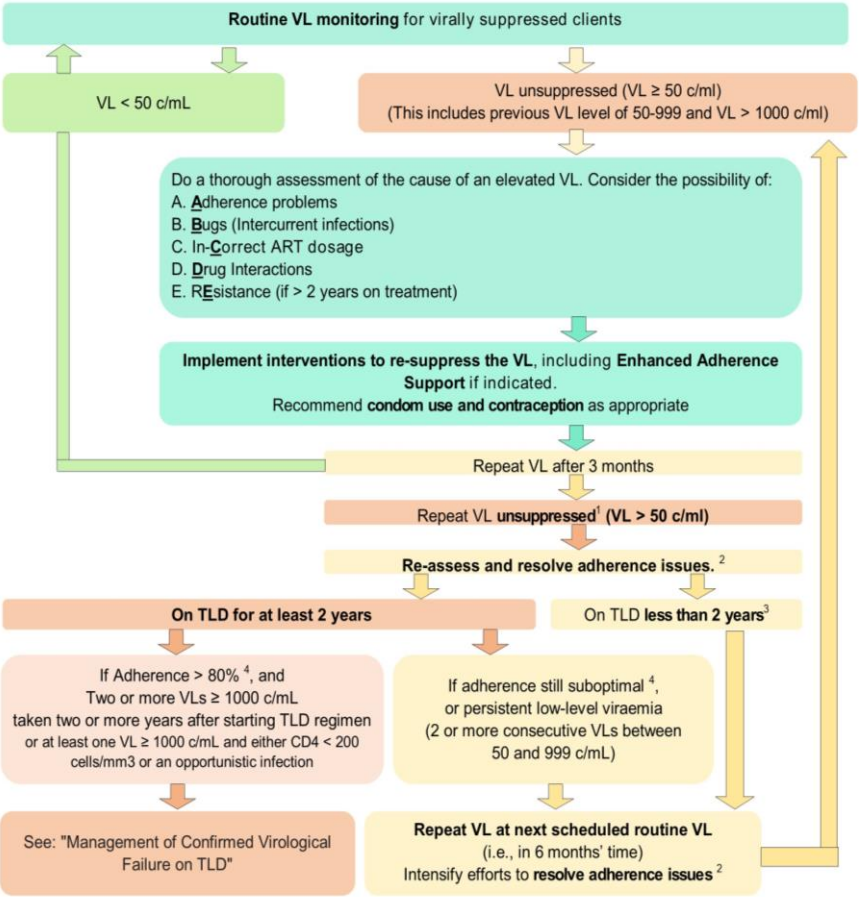
» Important information to assist in applying for third-line antiretrovirals can be found at www.righttocare.org/what-we-do/third-line-art/

Applications can be emailed to TLART@health.gov.za

General comments

Switch to tablets or capsules from syrups or solutions as soon as possible.
Use fixed-dose combinations in preference to single agents.
If available, use once daily regimens.

Viral Load Monitoring for clients on TLD



1. Due to their high genetic barrier, resistance to a first-line DTG-containing (TLD1) regimen is extremely rare. If other reasons for an unsuppressed VL have been addressed or excluded, e.g., drug interactions, and the client remains unsuppressed at their repeat VL, suboptimal adherence remains the most probable cause for non-suppression. The highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. 99,9% of these clients will re-suppress on TLD if adherent!
2. Repeat ABCDE assessment as outlined on "ABCDE assessment of an Elevated Viral Load" on page 20. Remember to ask about treatment side-effects, the potential cost of transport or loss of income related to clinic visits, non-disclosure, gender-based violence (GBV), and current or prior drug interactions. Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance.
3. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen. If necessary, discuss with an expert
4. Objective measures of good adherence include at least one of:
   a. Pharmacy refills > 80% in the last 6-12 months (if this is known)
   b. Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   c. Detection of current antiretroviral drug/s in the client's blood or urine, if available

Note: Self-reported adherence is not considered a measure of good adherence.

ART regimens for children with confirmed virological failure

All children and adolescents with confirmed virological failure should be discussed with an expert.

	NNRTI-based regimen	PI-based regimen[3]	InSTI-based regimen[3]		
Regimen	ABC/AZT/TDF + 3TC/FTC + EFV/NVP	AZT/TDF + 3TC/FTC + LPV/r or ATV/r	ABC/AZT/TDF + 3TC/FTC + DTG		
Resistance testing[4]	Resistance test not required.	Resistance test required.	Resistance test required.		
Resistance test results	Not applicable.	No PI resistance.	PI resistance (or genotype unsuccessful).	No InSTI resistance.	InSTI resistance.
New regimen or Other action required	If < 10 years and < 30 kg: AZT + 3TC + DTG	If < 10 years and < 30 kg: 2 NRTIs + DTG (1 active NRTI in consultation with an experienced practitioner in child ARV medicine.) Adherence issues must be addressed.	Refer to Third-Line Committee. Adherence issues must be addressed.	If < 10 years and < 30 kg: 2 NRTIs + DTG (1 active NRTI in consultation with an expert in child ARV medicine). Adherence issues must be addressed.	Refer to Third-Line Committee. Adherence issues must be addressed.
	If > 10 years and > 30 kg: TDF + 3TC + DTG[1,2]	If > 10 years and > 30 kg: TDF + 3TC + DTG.[1,2] Adherence must be addressed.		If > 10 years and > 30 kg: TDF + 3TC + DTG.[1,2] Adherence must be addressed.	

1. Always check hepatitis B status before stopping TDF. If the client has chronic hepatitis B, stopping TDF may lead to a severe hepatitis flare. If hepatitis B-positive, TDF should be continued in the second-line regimen.
2. Before switching to TDF, ensure renal function by checking eGFR/creatinine. (See Chapter 6: Nephrological/Urological Disorder, section 6.4: Acute Kidney Injury, for calculation).
3. See Transition to ABC/3TC/DTG.
4. Criteria for HIV Drug resistance (refer to the 2023 HIV Guidelines)

	Abacavir (ABC)	Lamivudine (3TC)	Abacavir + Lamivudine (ABC + 3TC)	Dolutegravir (DTG)	Dolutegravir when on rifampicin
Target dose	8 mg/kg **TWICE daily** **OR** If ≥ 10 kg: 16 mg/kg **ONCE daily**	4 mg/kg **TWICE daily** **OR** If ≥ 10 kg: 8 mg/kg **ONCE daily**	As for individual medications **ONCE daily**	By weight band **ONCE daily**	By weight band **TWICE daily**
Available formulations	Sol. 20 mg/mL Tabs 60 mg (scored, dispersible), 300 mg (not scored)	Sol. 10 mg/mL, Tabs 150 mg (scored)	Dispersible tablets (FDC): ABC/3TC 120/60 mg Tablet FDC: ABC/3TC 600/300 mg ABC/3TC/DTG 600/300/50 mg	Dispersible tabs (DT) 10 mg, film coated (FC) tabs 50 mg, FDC: TLD 300/300/50 mg **OR** ABC/3TC/DTG 600/300/50 mg **DT AND FC TABLETS ARE NOT BIOEQUIVALENT**	Dispersible tabs (DT) 10 mg, film coated (FC) tabs 50 mg, FDC: TLD 300/300/50 mg **OR** ABC/3TC/DTG 600/300/50 mg **DT AND FC TABLETS ARE NOT BIOEQUIVALENT**
Weight (kg)	Consult with a clinician experienced in paediatric ARV prescribing for neonates (< 28 days of age) and infants weighing < 3 kg.				
3–5.9	3 mL 12 hourly **OR** 1 x 60 mg tab 12 hourly	3 mL 12 hourly	1 x 120/60 mg tab daily	0.5 x 10 mg DT daily	0.5 x 10 mg DT 12 hourly
6-9.9	4 mL 12 hourly **OR** 1.5 x 60 mg tabs 12 hourly	4 mL 12 hourly	1.5 x 120/60 mg tabs daily	1.5 x 10 mg DT daily	1.5 x 10 mg DT 12 hourly
10–13.9	4 x 60 mg tabs daily **OR** 12 mL daily	12 mL daily	2 x 120/60 mg tabs daily	2 x 10 mg DT daily	2 x 10 mg DT 12 hourly

<table>
<tr><th></th><th>Abacavir
(ABC)</th><th>Lamivudine
(3TC)</th><th>Abacavir +
Lamivudine
(ABC + 3TC)</th><th>Dolutegravir
(DTG)</th><th>Dolutegravir when on rifampicin</th></tr>
<tr><td>14–19.9</td><td>5 x 60 mg tabs daily
OR
1 x 300 mg tab daily</td><td>1 x 150 mg tab daily</td><td>2.5 x 120/60 mg tabs daily</td><td>2.5 x 10 mg DT daily</td><td>2.5 x 10 mg DT
12 hourly</td></tr>
<tr><td>20–24.9</td><td>1 x 300 mg tab
PLUS
1 x 60 mg tab daily
OR
6 x 60 mg tabs daily</td><td rowspan="4">2 x 150 mg tabs daily</td><td rowspan="4">1 x ABC/3TC 600/300 mg tab daily
OR
ABC/3TC/DTG FDC (600/300/50 mg) if eligible, daily</td><td>3 x 10 mg DT daily
OR
1 x 50 mg FC tab daily</td><td>3 x 10 mg DT 12 hourly
OR
1 x 50 mg FC tab
12 hourly</td></tr>
<tr><td>25–29.9</td><td rowspan="3">2 x 300 mg tabs daily</td><td>1 x 50 mg tab daily
OR
FDC: ABC/3TC/DTG 600/300/50 mg tab daily</td><td>1 x 50 mg tab 12 hourly
OR
FDC: ABC/3TC/DTG 600/300/50 mg tab
12 hourly</td></tr>
<tr><td>30–39.9</td><td rowspan="2">1 x 50 mg FC tab daily
OR
FDC: TLD if eligible daily
OR
FDC: ABC/3TC/DTG if eligible daily</td><td rowspan="2">1 x 50 mg FC tab
12 hourly
OR
FDC: TLD if eligible daily + 50 mg DTG FC tab 12 hours later
OR
FDC: ABC/3TC/DTG if eligible daily + 50 mg DTG FC tab 12 hours later</td></tr>
<tr><td>≥ 40</td></tr>
</table>

	Lopinavir/ritonavir (LPV/RTV)	**Abacavir + Lamivudine + Lopinavir/ ritonavir**	**Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin)** ***Choose one of the 2 options below as appropriate***		**#Atazanavir (ATV) + ritonavir (RTV)**	**Efavirenz (EFV)**	**Zidovudine (AZT)**
Target dose	300/75 mg/m^2/dose LPV/RTV **TWICE daily**	By weight band **TWICE daily**	LPV/RTV std dose + super-boosting with ritonavir (RTV) powder **TWICE daily** (≥ 0.75 x LPV dose 12 hourly)	Double-dose LPV/RTV tabs ONLY if able to swallow whole LPV/RTV tabs **TWICE daily**	By weight band **ONCE daily**	By weight band **ONCE daily**	180–240 mg/m^2/dose **TWICE daily**
Available formulations	Sol. 80/20 mg/mL Adult tabs 200/50 mg, Paed tabs 100/25 mg **TABLETS MUST BE SWALLOWED WHOLE** Pellets 40/10 mg per capsule **ONLY FOR USE IF NOT TOLERATING LPV/RTV SOLUTION. CAPSULES ARE NOT RECOMMENDED < 6 MONTHS OF AGE**	Caps 30/15/ 40/10 mg **IF PATIENT IS ON RIFAMPICIN TB TREATMENT, ADD RTV POWDER** (next column)	Oral powder 100 mg per packet	Adult tabs 200/50 mg, Paed tabs 100/25 mg	ATV caps 150, 200 mg: RTV tabs 100 mg; FDC: ATV/RTV 300/100 mg; **RTV TABLETS AND ATV/R FDC TABLETS MUST BE SWALLOWED WHOLE**	Caps/tabs 50, 200, 600 mg; FDC: TEE 300/200/600 mg; **TABLETS MUST BE SWALLOWED WHOLE**	Sol. 10 mg/mL Tabs 100 mg, 300 mg (not scored), AZT/3TC 300/150 mg
Weight (kg)	Consult with a clinician experienced in paediatric ARV prescribing for neonates (< 28 days of age) and infants weighing < 3 kg.						

	Lopinavir/ritonavir (LPV/RTV)	Abacavir + Lamivudine + Lopinavir/ ritonavir	Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin) *Choose one of the 2 options below as appropriate*		#Atazanavir (ATV) + ritonavir (RTV)	Efavirenz (EFV)	Zidovudine (AZT)
3–5.9	*1 mL 12 hourly **OR** 2 capsules 12 hourly	2 capsules 12 hourly	LPV/RTV std dose **PLUS** oral RTV powder 100 mg (1 packet) 12 hourly	Do not use double-dose LPV/RTV tabs	Not recommended	Not recommended	6 mL 12 hourly
6–9.9	*1.5 mL 12 hourly **OR** 3 capsules 12 hourly	3 capsules 12 hourly					9 mL 12 hourly
10–13.9	2 mL 12 hourly **OR** 4 capsules 12 hourly **OR** 2 x 100/25 mg paed tabs in morning **PLUS** 1 x 100/25 mg paed tab at night	4 capsules 12 hourly	LPV/RTV std dose **PLUS** oral RTV powder 200 mg (2 packets) 12 hourly	3 x 100/25 mg tabs 12 hourly	ATV 1 x 200 mg cap daily **PLUS** RTV 1 x 100 mg tab or 100 mg oral powder (1 packet) daily	1 x 200 mg cap/tab at night	12 mL 12 hourly **OR** 1 x 100 mg tab 12 hourly
14–19.9	2.5 mL 12 hourly **OR** 5 capsules 12 hourly **OR** 2 x 100/25 mg paed tabs 12 hourly **OR** 1 x 200/50 mg adult tab 12 hourly	5 capsules 12 hourly		4 x 100/25 mg paed tabs 12 hourly **OR** 2 x 200/50 mg adult tabs 12 hourly		1 x 200 mg cap/tab + 2 x 50 mg caps/tabs at night	2 x 100 mg tab in morning **PLUS** 1 x 100 mg tab at night **OR** 15 mL 12 hourly

	Lopinavir/ritonavir (LPV/RTV)	Abacavir + Lamivudine + Lopinavir/ ritonavir	Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin) *Choose one of the 2 options below as appropriate*		#Atazanavir (ATV) + ritonavir (RTV)	Efavirenz (EFV)	Zidovudine (AZT)
20–24.9	3 mL 12 hourly **OR** 6 capsules 12 hourly **OR** 2 x 100/25 mg paed tabs 12 hourly **OR** 1 x 200/50 mg adult tab 12 hourly	6 capsules 12 hourly					2 x 100 mg tabs 12 hourly **OR** 20 mL 12 hourly
25–29.9	3.5 mL 12 hourly **OR** 7 capsules 12 hourly **OR** 3 x 100/25 mg paed tabs 12 hourly **OR** 1 x 200/50 mg adult tab 12 hourly **PLUS** 1 x 100/25 mg paed tab 12 hourly	Not recommended	LPV/RTV std dose **PLUS** oral RTV powder 300 mg (3 packets) 12 hourly	6 x 100/25 mg paed tabs 12 hourly **OR** 3 x 200/50 mg adult tabs 12 hourly	1 x ATV/RTV 300/100 mg FDC daily **OR** ATV 2 x 150 mg caps daily **PLUS** RTV 1 x 100 mg tab or 100 mg oral powder (1 packet) daily	2 x 200 mg caps/tabs at night	1 x 300 mg tab 12 hourly **OR** 1 x AZT/3TC 300/150 mg tab 12 hourly
30–39.9	5 mL 12 hourly **OR** 10 capsules 12 hourly **OR** 4 x 100/25 mg paed tabs 12 hourly			8 x 100/25 mg paed tabs 12 hourly **OR**			
≥ 40						2 x 200 mg caps/tabs at night **OR**	

	Lopinavir/ritonavir (LPV/RTV)	Abacavir + Lamivudine + Lopinavir/ ritonavir	Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin) *Choose one of the 2 options below as appropriate*		#Atazanavir (ATV) + ritonavir (RTV)	Efavirenz (EFV)	Zidovudine (AZT)
	OR 2 x 200/50 mg adult tabs 12 hourly			4 x 200/50 mg adult tabs 12 hourly		FDC: TEE if eligible, daily	

*Avoid LVP/r solution in any full-term infant < 14 days of age and any preterm infant < 42 weeks post conceptual age (corrected gestational age) or obtain expert advice.
Children weighing 25 to 29.9 kg may also be dosed with LPV/r 200/50 mg adult tabs: 2 tablets in the morning and 1 tablet at night.
#Atazanavir plus ritonavir should not be used in children/adolescents on treatment with rifampicin, obtain expert advice.
No dosage adjustments are required for children receiving treatment with efavirenz and rifampicin.

Specific information on ARVs		
	Storage	**Adverse effects**
Nucleoside reverse transcriptase inhibitors (NRTIs)		
Zidovudine (AZT)	Room temperature.	» Haematological, e.g. anaemia, neutropenia.
Dolutegravir (DTG)	Room temperature.	» Insomnia – rare.
Lamivudine (3TC)	Room temperature.	» Pure red cell aplasia – uncommon.
Abacavir (ABC)	Room temperature.	» Abacavir Hypersensitivity Reaction: » Very rare in our population: > usually occurs in first 6 weeks of initiation of therapy, > symptoms and signs become worse with each subsequent dose, > multi-system manifestations, > fever, and rash common, > other systems include gastrointestinal signs (nausea, vomiting, abdominal pain) and respiratory symptoms (dyspnoea, sore throat and cough). » Laboratory abnormalities include raised transaminases and creatinine phosphokinase, and lymphopenia. » **Discuss with an expert. If ABC discontinued, do not re-challenge with abacavir.**
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)		
Nevirapine (NVP)	Room temperature.	» Skin rash usually occurs in first 6 weeks. » Do not increase the dosage until the rash resolves. » Beware of liver toxicity.
Efavirenz (EFV)	Room temperature	» Give at night to avoid CNS side effects: > dysphoria > vivid dreams > dizziness > distracted » Hepatotoxicity » Breast enlargement in males and females.

Specific information on ARVs		
	Storage	**Adverse effects**
Protease inhibitors (PIs)		
Ritonavir (r)	Tablets/ powder – room temperature.	» Bitter taste.
Lopinavir/ ritonavir (LPV/r)	Syrup – refrigerator. Tablets/ pellets and granules – room temperature.	» Nausea » Vomiting » Diarrhoea

Important side effects of ARVs

*(*Consult an expert before stopping ART)*

	Continue ART with careful monitoring.	**Consult an expert and/or stop treatment.**
Anaemia	» Hb: 7.0–9.9 g/dL	» Hb < 7 g/dL or cardiac failure
Neutropenia	» 0.4–1.2 x 10^9/L	» ≤ 0.399 x 10^9/L
Increased liver enzymes and hepatitis	» ≤ 9.9 x upper normal limit	» ≥ 10.0 x upper normal limit
Increased serum triglycerides	» 1.54–8.46 mmol/L	» ≥ 8.47 mmol/L*
Increased cholesterol	» 4.43–12.92 mmol/L	» ≥ 12.93 mmol/L*
Severe skin reactions	» diffuse maculo-papular rash, or » dry desquamation	» vesiculation, or » ulcers, or » exfoliative dermatitis, or » Stevens-Johnson syndrome, or » erythema multiforme, or » moist desquamation, or » with elevated ALT or AST
» Peripheral neuropathy » Myopathy » Abdominal pain » Nausea and vomiting » Pancreatitis » Headache » Fatigue » Sedative effect » Sleep disturbance » Confusion » Abnormal thinking	Clinical evaluation: » Discuss all cases urgently with an HIV expert before interrupting therapy.	

Criteria for changing therapy

Adverse effects

Children may occasionally need to change antiretroviral drugs because of intolerance or a serious adverse reaction. There is no need to change an entire regimen for a single adverse drug reaction.

Note: A single drug substitution can only be made if the viral load is < 50 copies/mL/undetectable or if the change is made in the first 6 months of starting a regimen. The decision to swap must be made by a doctor with antiretroviral experience (this can be by telephonic consultation), as inappropriate choices of antiretrovirals may be ineffective or dangerous.

Treatment failure

The HIV viral load is the most sensitive method to detect failure of response to ART.

Virological failure can be defined as a measurable viral load despite optimal adherence and dosage over 4 months. Treatment failure is primarily defined by viral loads, as waiting for clinical or immunological failure increases the chances of increasing viral resistance to other available antiretroviral agents.

Poor adherence is the most common cause of treatment failure. Adherence issues should be assessed and then implement strategies to improve adherence.

» For guidance on the step-up adherence package, refer to the National adherence guidelines.

https://www.nacosa.org.za/wp-content/uploads/2016/11/Integrated-Adherence-Guidelines-NDOH.pdf

REFERRAL

» Complicated or very ill children should be referred to a practitioner skilled in the care of such children.
» Attempts should be made to refer patients to accredited primary health care sites once stable on ART.

9.2 TUBERCULOSIS AND HIV

B20.0

DESCRIPTION

TB and HIV are often comorbid conditions. Exclude TB by a history of TB contacts, clinical examination, chest X-ray, tuberculin skin test (TST), or lateral flow urine lipoarabinomannan (TB-lam), *M tuberculosis* PCR test and mycobacterial culture (where TB disease is suspected on clinical or radiological grounds) in all patients before starting ART. Every attempt should

be made to obtain microbiologic specimens for TB testing (sputum, NGAs or other, as applicable), as this presents the opportunity to prove TB disease in the child.

Re-evaluate the risk for TB and TB contacts at each visit on history (including contact history) and clinical examination.

MEDICINE TREATMENT

TB prophylaxis

Give TB prophylaxis to all HIV-infected children exposed to close contact with an infectious pulmonary TB case (sputum microscopy smear-positive, culture-positive or *M tuberculosis* PCR test positive) or TST **but** in whom no evidence of TB disease is present.

- Isoniazid, oral, 10 mg/kg/dose once daily for 6 months.
  - Maximum dose: 300 mg daily.

Repeat the course if an HIV-infected patient, irrespective of age, is re-exposed to a TB contact at any point after completing TB treatment or prophylaxis.

If the patient has been exposed to a known MDR-TB or XDR-TB source case or the contact case has failed standard TB treatment, refer for an expert opinion. See Chapter 10: Tuberculosis, section 10.2: Tuberculosis, pulmonary in children.

TB treatment

<u>If the child is not yet on ART</u>:

» TB treatment and ART can be started at the same time, with the exception of children with TB meningitis – start ART at 4 weeks regardless of CD4 count to avoid IRIS.
» Assess the child for possible disseminated TB disease.
» Be aware of the possibility of Immune Reconstitution Inflammatory Syndrome (IRIS).

<u>If the child is already on ART</u>:

» Commence TB treatment, considering possible drug interactions and the need for ART dosage adaptations.

<u>If the child needs to take concomitant ART and rifampicin-containing treatment</u>:

- Dolutegravir: use dolutegravir twice daily.
- Efavirenz: use the normal recommended dosage as per the dosing table.
- Abacavir and lamivudine: no adjustment of dosages.
- Lopinavir/ritonavir: refer to the dosage table for the ritonavir boosting doses.
- <u>Avoid using double-dose lopinavir/ritonavir solution in young children</u>. If ritonavir powder is not available, consult an expert.

- Give pyridoxine (vitamin B_6) to all children on TB and ARV treatment due to shared toxicities of the regimens.

9.3 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

D89.3

DESCRIPTION

Clinical deterioration can occur after starting ART due to an improvement in the immune system's response to organisms already causing infection, e.g.

- *M bovis BCG,*
- *M tuberculosis (MTB),*
- *M avium complex,*
- *M leprae,*
- *P jiroveci,*
- CMV,
- JC virus.
- *C neoformans,*
- *Aspergillus*,
- *C albicans,*
- Human Herpes viruses,
- Human Papilloma virus,
- Hepatitis B and C viruses (HBV, HCV),

There are two manifestations of IRIS:

1. Unmasking occurs when a previously unsuspected condition manifests.
2. Paradoxical, i.e. a known condition on appropriate treatment worsens.

DIAGNOSTIC CRITERIA

» Exclude other active or inadequately treated diseases (including MDR-TB).
» Ensure adherence to the prescribed therapy.
» Presentation:
  > Usually during the first 6 weeks after starting ART.
  > Clinical presentation depends on the causative organism and the organ system involved, e.g. TB presents with fever, lymph–adenopathy, worsening of the original tuberculous lesion, and/or deteriorating chest radiographic manifestations such as a miliary pattern or pleural effusion.

MEDICINE TREATMENT

Treat underlying disease aggressively.
Antimicrobial therapy for specific infections.

In severe reactions:

- Prednisone, oral, 1.5 mg/kg daily for 2 weeks, followed by 0.75 mg/kg daily for 2 weeks.

Usually, ART is continued, and the underlying condition is managed.
Local IRIS with *M bovis BCG* usually does not require antimicrobial therapy.

9.4 POST-EXPOSURE PROPHYLAXIS FOLLOWING ALLEGED PENETRATIVE SEXUAL ABUSE

See Standard Treatment Guidelines and Essential Medicines List for Primary Health Care.

9.5 HIV IN ADOLESCENCE

B20-24

DESCRIPTION

Adolescence encompasses the period of physical and psychological development from the onset of puberty to maturity. HIV in adolescents may be due to:

1. Vertical infection in infancy that presents as long-term non-progressors; or
2. Sexually acquired HIV from unprotected intercourse.

Increasing numbers of perinatally infected infants are surviving to adolescence.

Adolescence is a high-risk period for non-adherence to therapy.
Mood disorders, denial, peer pressure, self-esteem and suicide risk are more common, and patients may need to be referred for psychological support.

Education about sexual and reproductive health should be commenced early. Every encounter with the adolescent needs to be maximally utilised to discuss condom and contraception use to protect against unplanned pregnancies and STI transmission, including HIV. Schools should be taking an active role in this education. Sexually active youth need to be screened for STI symptoms and managed appropriately.

Consent

The current acts and regulations should be followed for testing, treatment and disclosure.

Disclosure

All adolescents need to be aware of their HIV status. This should be handled sensitively. In addition, disclosure of diagnosis has ramifications for adherence. Disclosure should be planned with the caregiver and usually takes place over 2–3 visits. Disclosure should start in childhood using non-specific terms such as ‘germ’ and ‘medicine’, building up to full disclosure around 10 years of age. Intervention by a social worker is useful where appropriate, although skilled counsellors often manage disclosure. Determine what the adolescent already knows and discuss with the caregiver who should disclose it and where.

Dosage of ARVs

In children over the age of 10 years and over 30 kg, use adult dosage regimens – consult ART guidelines.[1]

The transition from paediatric ART regimens to adolescent/adult regimens:

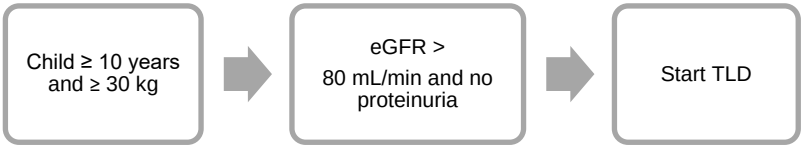
» Adolescents with an undetectable VL (< 50 copies/mL) and no side effects on ABC + 3TC + DTG can remain on the same regimen until the patient becomes eligible for the TDF + 3TC + DTG (TLD FDC) at 10 years of age and weighing ≥ 30 kg.

» When an adolescent reaches 10 years of age and is ≥ 30 kg, a creatinine level, calculation of the estimated glomerular filtration rate (eGFR) using a standard formula, and urine strip test should be performed.

> If the eGFR is > 80 mL/min and there is no proteinuria on a urine strip test, the patient can be switched to TDF + 3TC + DTG (TLD FDC).

> If the eGFR is < 80 mL/min or there is > 1+ proteinuria on a urine strip test, then refer to an expert for advice before switching.

Transition from child to adolescent regimen



Contraception in HIV-infected adolescents on ART

Hormonal contraceptives and IUCDs do not prevent sexually transmitted infections. Additional use of condoms is required.

- Intra-uterine contraceptive device (IUCD): HIV is not a contraindication to IUCD use and may be used in adolescents on ART, e.g. 380 mm^2 copper – standard type.
- Progestogen-only subdermal implant contraceptive, e.g. levonorgestrel, 150 mg, subdermal two-rod implant.

Note: Progestogen-only subdermal implant should NOT be used in patients on efavirenz. Additional non-hormonal contraception is required during and for up to 28 days after discontinuation of enzyme-inducing agents, including rifampicin, efavirenz, and many anticonvulsants (e.g. carbamazepine, phenobarbital, phenytoin).

LoE II[7,8]

- Injectable contraception: e.g. medroxyprogesterone acetate (long-acting), IM, 150 mg, 12 weekly.

Note: It is unnecessary to shorten the dosage interval for women taking concomitant enzyme-inducing drugs, e.g. rifampicin, antiretrovirals and anticonvulsants.

» Combined oral contraceptives (COCs) are indicated for motivated patients where adherence is more likely but are associated with drug-drug interactions.

References

[1] South African National Department of Health. 2023 Antiretroviral Therapy Clinical Guidelines for the Management of HIV in Adults, Pregnancy and Breastfeeding, Adolescents, Children, Infants and Neonates. April 2023.
[2] Nielsen-Saines K, et. al. Three Postpartum Antiretroviral Regimens to prevent Intrapartum HIV infection. NEJM. 2012;366:2368-2379.
[3] Capparelli EV, and Pediatric AIDS Clinical Trials Group 331 Investigators. Pharmacokinetic and tolerance of zidovudine in preterm infants. Journal of Pediatrics. 2003, January; 142 (1):47-52.
[4] Mirochnick M, Capparelli E, Connor J. Pharmacokinetics of zidovudine in infants: a population analysis across studies. Clinical Pharmacology and Therapeutics. 1999, July;66(1):16-24.
[5] Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf.
[6] The health and human services panel on treatment of HIV-infected pregnant women and prevention of perinatal transmission - A working group of the office of AIDS research advisory Council. Guidelines for the use of Antiretroviral Agents in Pediatric HIV Infection. http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf.
[7] Perry SH, et.al. Implementing the Jadelle implant for women living with HIV in a resource-limited setting: concerns for drug interactions leading to unintended pregnancies. AIDS. 2014; 28(5):791-793.
[8] Vieira CS, et.al. Effect of antiretroviral therapy including lopinavir/ritonavir or efavirenz on etonogestrel-releasing implant pharmacokinetics in HIV-positive women. J Acquir Immune Defic Syndr. 2014; 66(4):378-385.