CHAPTER 9

HUMAN IMMUNODEFICIENCY VIRUS INFECTION

9.1 HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS

B20–24

Comprehensive guidelines are available for ART and the care of children with HIV infection in the 2019 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates[1]; and the 2018 Guideline for the Prevention of Mother to Child Transmission of Communicable Infections (HIV, Hepatitis, Listeriosis, Malaria, Syphilis and TB).[2]

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 transmitted from mother to child, but in adolescents and adults, sexual transmission is the usual route for new infections.

Infants born to HIV-infected mothers 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): 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 in 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).
» **Symptomatic child/infant:** If at any time the child has evidence suggesting HIV infection, 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:

» Always do a HIV rapid/ELISA test (HIV rapid test for ALL children 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 kit of a different manufacturer, and 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 National Department of Health Guideline 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.

Transmission of HIV infection from mother to child may occur during pregnancy, during delivery, or via breastfeeding. Prevention of mother to child transmission (PMTCT) 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 this information must be available at the time of delivery to ensure the correct PMTCT intervention is given to the infant.

With the effective use of antiretrovirals, the risk of HIV transmission through breastfeeding is minimised. In situations where the viral load of the mother cannot be suppressed, the risk of breast milk transmission remains significant.

The PMTCT plan starts with initiation of ART in the mother (either pre- or post-conception), thereafter, at delivery, the HIV-exposed infant may be classified into one of the following categories, which determines the appropriate infant prophylaxis regimen:

- Low risk.
- High risk.

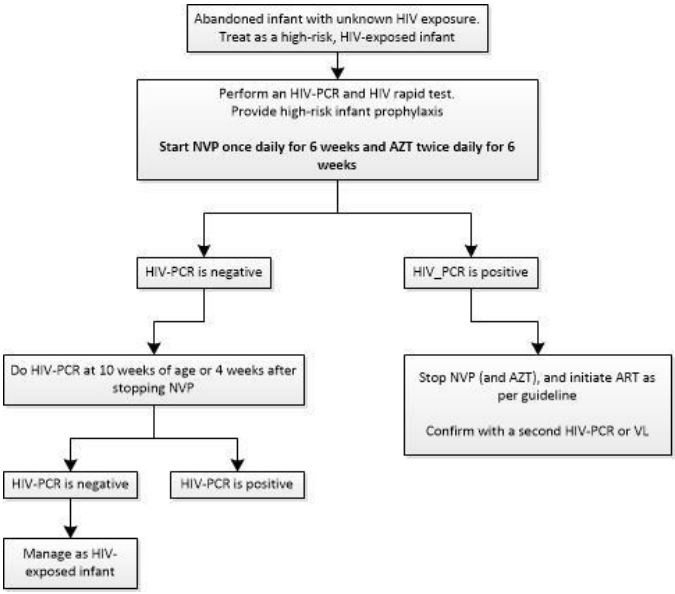
MANAGEMENT OF HIV-EXPOSED INFANTS

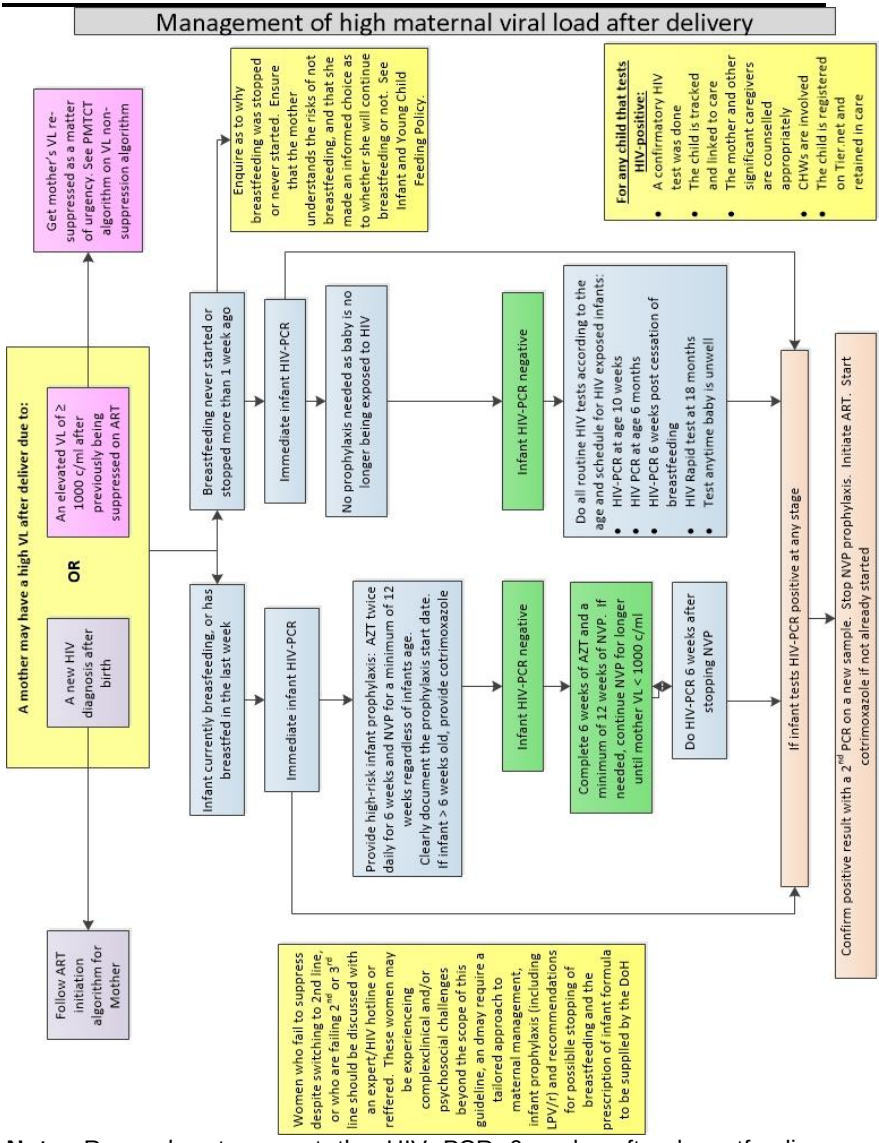
Situation*	Feeding advice	Comment
LOW RISK **NVP** at birth and then daily for 6 weeks.		
Mother booked early in ANC and is adherent to treatment, maternal VL < 1000 copies/mL (most recent VL taken during the last 12 weeks of antenatal care), **OR** Maternal VL < 1000 copies/mL at delivery.	» Encourage breastfeeding.	» Do HIV PCR at birth. » Do HIV PCR at 10 weeks. » Do HIV PCR at 6 months. » Do infant HIV testing 6 weeks post-cessation of breastfeeding (either HIV PCR or ELISA depending on age). » Encourage maternal ART adherence.

Situation*	Feeding advice	Comment
HIGH RISK *(Initiate as soon as possible)* **NVP** daily for at least 12 weeks **and AZT** twice daily for 6 weeks.		
Mother with a VL of ≥ 1000 copies/mL (most recent VL taken during the last 12 weeks of antenatal care), or a mother with no VL result or no ART in the last 12 weeks. **OR** Maternal VL ≥ 1000 copies/mL at delivery. **OR** Breastfeeding mother diagnosed HIV-positive > 72 hours after delivery. **OR** No VL in last 12 weeks	Infants of mothers failing on 1st line treatment: » Encourage breastfeeding. Infants of mothers on 2nd or 3rd line regimens and VL > 1000 copies/mL: » Advise not to breastfeed. » Prescribe replacement feeding.	» Manage maternal HIV care as per ARV and PMTCT guidelines[1,2] » Do infant HIV PCR at birth/ immediately; if infant tests HIV PCR positive, repeat the HIV PCR test and initiate ART immediately. » Do HIV PCR at 10 weeks » Do HIV PCR at 6 months. » Do infant HIV testing 6 weeks post cessation of breastfeeding (either HIV PCR or ELISA depending on age). » Encourage maternal ART adherence. » If maternal VL ≥ 1000 copies/mL continue infant NVP prophylaxis.

***Non-breastfeeding mother diagnosed HIV-positive > 72 hours after delivery:** Do not start NVP. Perform an HIV test on the infant and, if positive, initiate ART.*

Unknown maternal status





Note: Remember to repeat the HIV PCR 6 weeks after breastfeeding cessation for all breastfed infants if < 18 months and repeat an HIV rapid/ ELISA test if ≥ 18 months.

LoE I[3]

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

Nevirapine (NVP) and Zidovudine (AZT) doses for infant on PMTCT
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 the NVP and AZT administration.
» Repeat the dose if baby vomits.
» If the infant HIV PCR is positive at any time, stop NVP and AZT, perform a second HIV PCR test and initiate ART immediately. Continue normal breastfeeding.

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

Infant Age/Wt	NVP Dose (Daily)	AZT Dose (Twice daily)
Birth–6 weeks		
2.0–2.49 kg	1 mL (10 mg) daily	1 mL (10 mg) twice daily
> 2.5 kg	1.5 mL (15 mg) daily	1.5 mL (15 mg) twice daily
6 weeks–6 months		
	2 mL (20 mg) daily	6 mL (60 mg) twice daily

Children > 6 months of age requiring prophylaxis should use treatment doses.

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

Weight	1st 2 weeks after birth (mg of NVP)	After 1st 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 < 1.9 kg	3.5 mg	6 mg
If the infant at 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[4,5,6]

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 commenced on the appropriate oral infant prophylaxis regimen. Ideally gestational age should be used to determine optimal dose.

Gestational Age	Approximate birth weight	AZT IV dosing for 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

Recommended Intervals for Infant and Child Testing	
HIV PCR test	**Rapid HIV Antibody test**
At Birth » All HIV-exposed neonates. **At 10 weeks** » All HIV-exposed infants. **At 6 months** » All HIV-exposed infants. 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.	**At 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). **Note:** Patients already on ART should not have a repeat HIV antibody test. **Breastfed infants: (6 weeks post cessation of breastfeeding)** » All HIV-exposed infants – age appropriate: < 18 months old – do an HIV PCR. ≥ 18 months old – do a rapid HIV antibody test (confirm HIV test in children between 18–24 months with an HIV PCR). **HIV testing should be offered to all children as well as their family and caregivers**.

If HIV PCR is indeterminate or discordant refer to: 'Recommendations for the management of indeterminate HIV PCR results within South Africa's early infant diagnosis programme[7]': https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5843082/.

Feeding advice

» Exclusive breastfeeding is strongly recommended for the first 6 months, after which, the nutritional requirements of the child will require the introduction of complementary foods, in addition to breastfeeding.
» Except where a mother is shown to be failing ART, the advantages of breastfeeding exceed the risks of HIV transmission in a mother on ART and the mother should be encouraged to breastfeed.
» 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. It can be used as an interim measure, for instance during maternal mastitis.

Cotrimoxazole prophylaxis

Indications:

- Sub-classification for HIV exposed uninfected infants at 10 week PCR test:
  » Babies born to mothers that are not virally suppressed (high-risk exposures) should be given cotrimoxazole from 6 weeks of age until the result of their 10-week PCR test is available. If 10-week PCR is negative and the mother remains not virally suppressed or engaging in mixed feeding, continue cotrimoxazole prophylaxis until HIV status confirmed; however if mother is virally suppressed discontinue use of cotrimoxazole prophylaxis.
  » Babies born to mothers who are adherent with their ART regimen and are virally suppressed (low risk setting) should not be given cotrimoxazole if Birth PCR is negative. Cotrimoxazole should only be initiated in the unlikely situation that such babies are subsequently confirmed to be HIV infected.
  » Babies with a positive HIV PCR should be started or continued on cotrimoxazole prophylaxis as per current guideline.

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

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)
2.5 to 4.9 kg	100/20 mg	2.5 mL	¼ tablet	–
5 to 13.9 kg	200/40 mg	5 mL	½ tablet	–
14 to 29.9 kg	400/80 mg	10 mL	1 tablet	½ tablet
> 30 kg	800/160 mg	–	2 tablets	1 tablet

If HIV-infected, 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

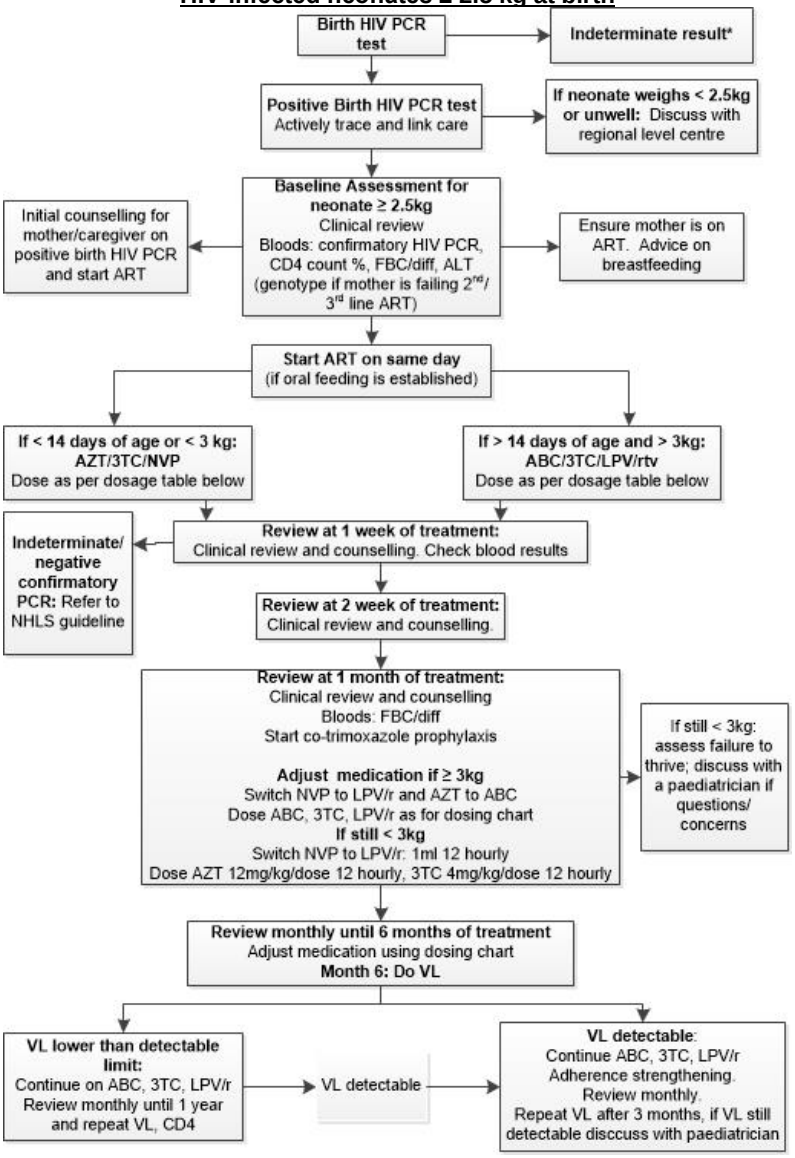
DESCRIPTION

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 allowance for flexibility after discussion with an expert.

Protocol for initiation of ART at < 4 weeks of age: HIV-infected neonates ≥ 2.5 kg at birth



*Refer to 'Recommendations for the management of indeterminate HIV PCR results within South Africa's early infant diagnosis programme[7]':
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5843082/

ARV drug dosing chart:
If < 14 days of age and weighing ≥ 2.5 kg at birth

	Lamivudine (3TC)		Zidovudine (AZT)		Nevirapine (NVP)	
Target dose	2 mg/kg/dose TWICE daily		4 mg/kg/dose TWICE daily		6 mg/kg/dose TWICE daily	
Available formulation	10 mg/mL		10 mg/mL		10 mg/mL	
Weight (kg)	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**
≥ 2.5–< 3.0	0.5 mL 12 hourly	5 mg 12 hourly	1 mL 12 hourly	10 mg 12 hourly	1.5 mL 12 hourly	15 mg 12 hourly
≥ 3.0–< 4.0	0.8 mL 12 hourly	8 mg 12 hourly	1.5 mL 12 hourly	15 mg 12 hourly	2 mL 12 hourly	20 mg 12 hourly
≥ 4.0–< 5.0	1 mL 12 hourly	10 mg 12 hourly	2 mL 12 hourly	20 mg 12 hourly	3 mL 12 hourly	30 mg 12 hourly

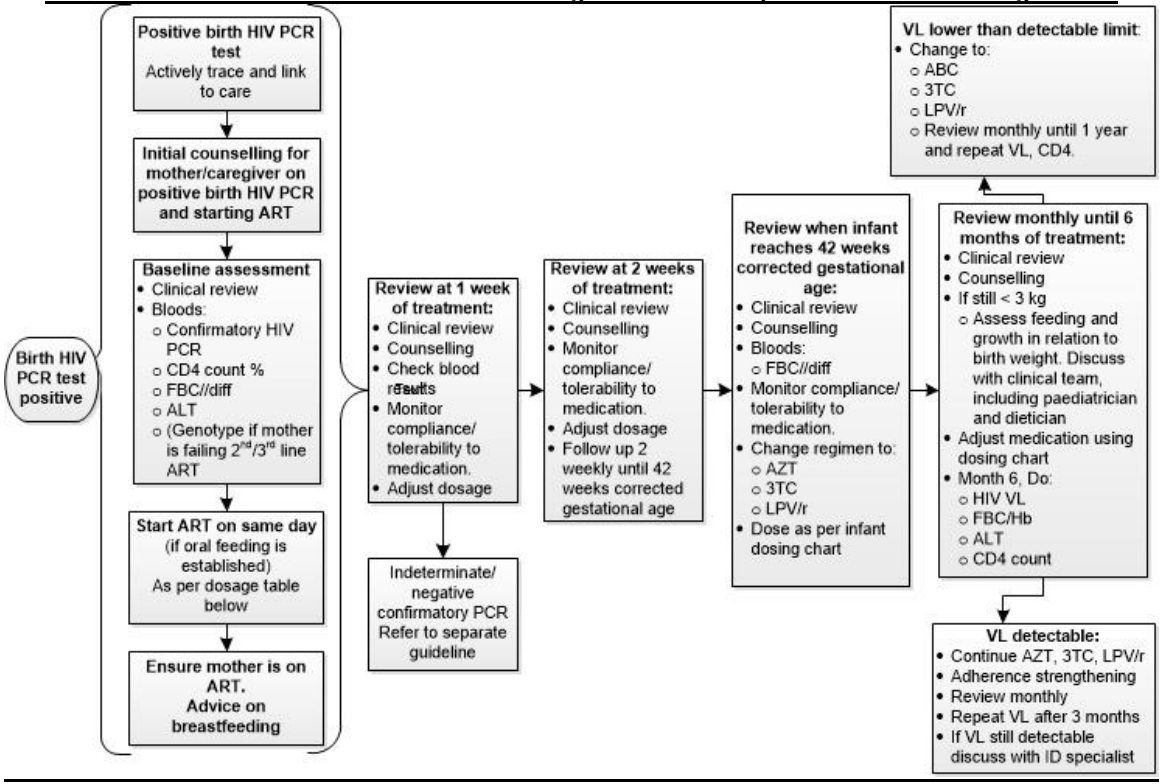
ARV drug dosing chart:
If > 14 days of age and weighing ≥ 3 kg

	Lamivudine (3TC)		Abacavir (ABC)		Lopinavir/ritonavir (LPV/rtv)	
Target dose	2 mg/kg/dose TWICE daily		8 mg/kg/dose TWICE daily		300/75 mg/m^2/dose TWICE daily	
Available formulation	10 mg/mL		20 mg/mL		80/20 mg/mL	
Weight (kg)	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**
≥ 3.0–< 4.0	0.8 mL 12 hourly	8 mg 12 hourly	0.5 mL 12 hourly	14 mg 12 hourly	0.8 mL 12 hourly	64/16 mg 12 hourly
≥ 4.0–< 5.0	1 mL 12 hourly	10 mg 12 hourly	0.6 mL 12 hourly	12 mg 12 hourly	1 mL 12 hourly	80/20 mg 12 hourly

Caregivers who will be 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 used to mark the correct dose on the syringe.

LoE III[8]

Protocol for initiation of ART at < 4 weeks of age: HIV-infected preterm infants < 2.5 kg at birth



ARV drug dosing chart:
For preterm infants < 42 weeks corrected gestational age

<table>
<tr><th>Drugs</th><th colspan="2">Lamivudine (3TC)</th><th colspan="2">Zidovudine (AZT)</th><th colspan="2">Nevirapine (NVP)</th></tr>
<tr><td>< 30 weeks</td><td colspan="2">2 mg/kg twice daily</td><td colspan="2">2 mg/kg twice daily</td><td colspan="2">2 mg/kg twice daily</td></tr>
<tr><td rowspan="2">30–35 weeks</td><td colspan="2" rowspan="2">2 mg/kg twice daily</td><td>Day 0–14</td><td>2 mg/kg twice daily</td><td colspan="2" rowspan="2">2 mg/kg twice daily</td></tr>
<tr><td>Day > 14</td><td>3 mg/kg twice daily</td></tr>
<tr><td rowspan="3">> 35 weeks</td><td>2–< 3 kg</td><td>0.5 mL twice daily</td><td>2–< 3 kg</td><td>1 mL twice daily</td><td>Day 0–14</td><td>4 mg/kg twice daily</td></tr>
<tr><td rowspan="2">3–< 4 kg</td><td rowspan="2">0.8 mL twice daily</td><td>3–< 4 kg</td><td>1.5 mL twice daily</td><td rowspan="2">Day > 14</td><td rowspan="2">6 mg/kg twice daily</td></tr>
<tr><td>4–< 5 kg</td><td>2 mL twice daily</td></tr>
</table>

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 the 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 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 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 CD count < 200 cells/mm^3 or WHO Stage 2–4.
Hb or FBC if available.	To detect anaemia or neutropenia.
At initiation of ART (baseline)	**Purpose**
Hb or FBC.	If less than 8 g/dL, manage appropriately.
CD4 count (if not performed in 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 meets criteria to stop cotrimoxazole. Thereafter, stop CD4 count monitoring if patient remains virologically supressed. If not virologically supressed monitor CD4 count every 6 months.	To monitor response to ART and stop cotrimoxazole prophylaxis as indicated.
Viral load (VL): At month 6 on ART, after 12 months on ART, then every 12 months.	To monitor viral suppression on ART. To identify treatment failure and identify adherence problems.
Hb or FBC and differential WBC at months 3 and 6 if on AZT. Thereafter, repeat if clinically indicated.	To identify AZT-related anaemia.
Cholesterol + triglyceride at month 3. If above acceptable range, do fasting cholesterol and TGs; and if still above acceptable range, obtain expert advice.	To monitor for PI-related metabolic side effects.

MEDICINE TREATMENT

Cotrimoxazole prophylaxis

Indications:

- Sub-classification for HIV exposed uninfected infants at 10 week PCR test:
  - » Babies born to mothers that are not virally suppressed (high-risk exposures) should be given cotrimoxazole from 6 weeks of age until the result of their 10-week PCR test is available. If 10-week PCR is negative and the mother remains not virally suppressed or engaging in mixed feeding, continue cotrimoxazole prophylaxis until confirmation of HIV status; however if mother is virally suppressed discontinue use of cotrimoxazole prophylaxis.
  - » Babies born to mothers who are adherent with their ART regimen and are virally suppressed (low risk setting) should not be given cotrimoxazole if Birth PCR is negative. Cotrimoxazole should only be initiated in the unlikely situation that such babies are subsequently confirmed to be HIV infected.
  - » Babies with a positive HIV PCR should be started or continued on cotrimoxazole prophylaxis as per current guideline.

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

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 2 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.

The preparation of 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 prognosis of the child.

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 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 on adherence. Social challenges should be overcome and not be barriers to care.

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

» Mandatory component: at least one identifiable caregiver able to 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 may facilitate adherence.

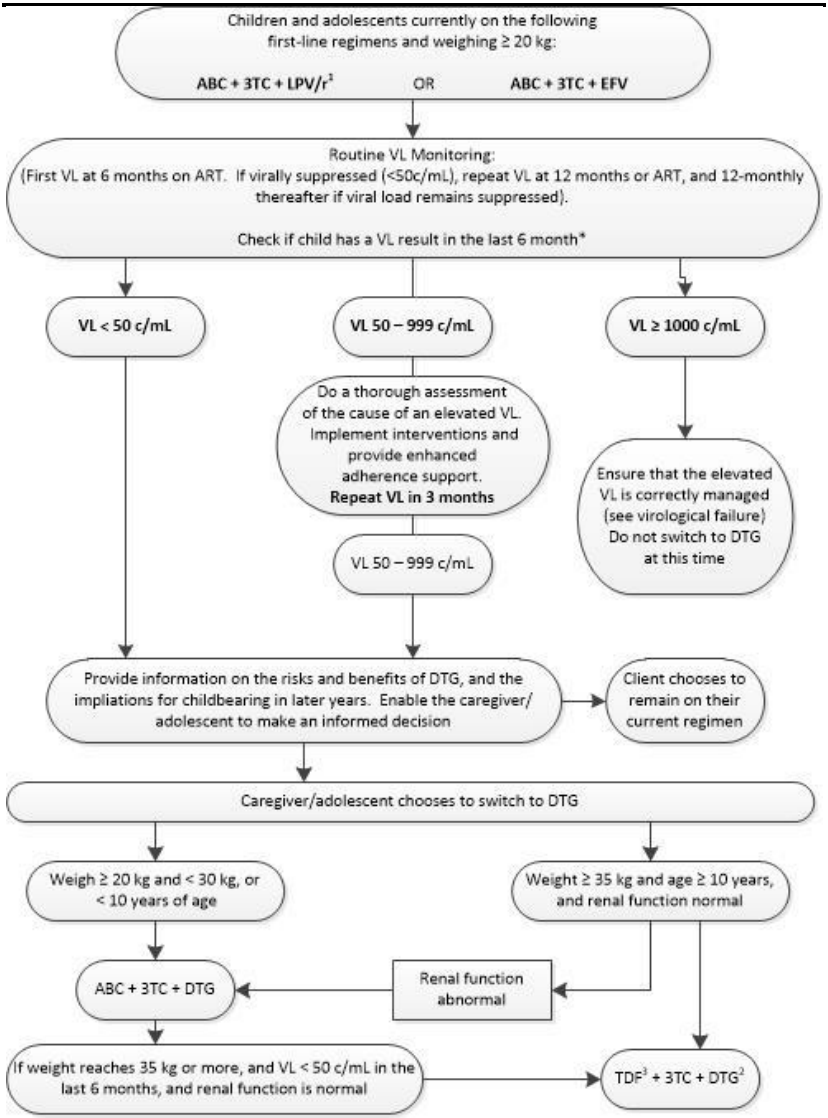
Requirements before ART is used

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

» that antiretroviral therapy is lifelong,
» 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

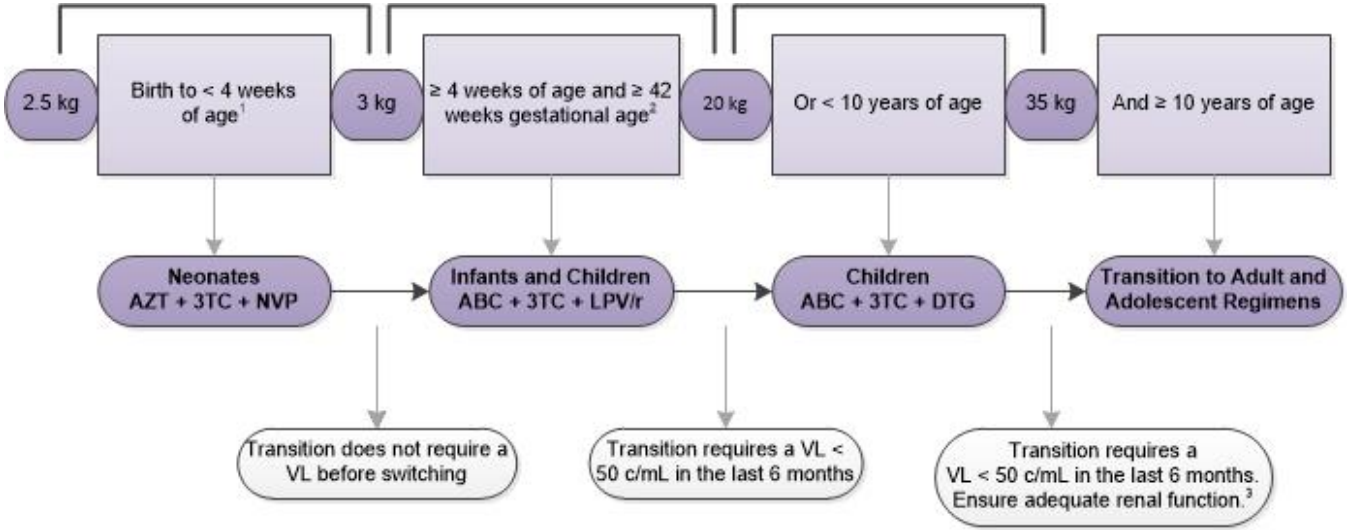
» Are chosen according to age, weight, expected adverse effects, efficacy and prior antiretroviral exposure.
» Adjust the dosage of antiretroviral therapy according to weight during follow-up visits. Assess weight gain and need for adjustment at each visit.
» Do not change regimens or move to second-line therapy without clear guidance from an experienced practitioner in child ARV medicine, as unnecessary loss of effective regimens can shorten life expectancy. Adherence problems need to be addressed thoroughly before switching to a second- or third-line regimen.
» Single drug substitution may only be made when drug-specific adverse effects are encountered, on condition that complete virological suppression is documented and the matter is discussed with an experienced practitioner in child ARV medicine first.



* If no VL test has been done in the last 6 months, additional VL testing outside of the routine VL monitoring schedule should NOT be done. Await results of routine annual VL test to determine eligibility to switch to DTG.

1. Switching LPV/r to DTG in this regimen applies strictly to first-line regimens only. If ABC + 3TC + LPv/r is used as a second-line regimen, it is possible that both NRTIs in the regimen are inactive. DTG should not be used without at least 1 active NRTI. If DTG is to be considered within a second-line regimen, expert guidance should be sought to ensure that a least 1 NRTI is active.
2. Discuss and provide sexual and reproductive health services for the sexually active adolescent.
3. Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine. (See Chapter 6: Nephrological/Urological Disorder, section 6.4: Acute Kidney Injury, for calculation).

First-Line Regimen
Neonates, Infants and Children 0 to < 10 years of age



1. For preterm neonates and neonates with birth weight < 2.5 kg, or neonates with severe anaemia, obtain advice from an expert or helpline.
2. For infants ≥ 4 weeks of age, ≥ 42 weeks gestational age, but weighing less than 3 kg, a paediatric expert should be consulted to determine the appropriate regimen.
3. 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).

Second- and Third-line ART Regimens for Children and Adolescents with Confirmed Virological Failure

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

<table>
<tr><th></th><th colspan="2">NNRTI-based Regimen</th><th colspan="3">PI-based Regimen for > 2 years</th><th colspan="2">InSTI based Regimen for > 2 years</th></tr>
<tr><td>Regimen</td><td colspan="2">ABC/AZT/TDF +3TC/FTC +EFV/NVP</td><td colspan="3">ABC/AZT/TDF + 3TC/FTC + LPV/r or ATV/r</td><td colspan="2">ABC/AZT/TDF + 3TC/FTC + DTG</td></tr>
<tr><td>Resistance testing</td><td colspan="2">Resistance test not required.</td><td colspan="3">Resistance test required.</td><td colspan="2">Resistance test required.</td></tr>
<tr><td>Resistance test results</td><td colspan="2">Not applicable.</td><td colspan="2">No PI resistance.</td><td>PI resistance (or genotype unsuccessful).</td><td>No InSTI resistance.</td><td>InSTI resistance.</td></tr>
<tr><td>Weight</td><td>< 20 kg</td><td>≥ 20 kg</td><td>< 20 kg</td><td>≥ 20 kg</td><td>All</td><td colspan="2">All children/adolescents on DTG will be ≥ 20 kg.</td></tr>
<tr><td rowspan="2">New regimen or Other action required</td><td rowspan="2">ABC/AZT + 3TC + LPV/r[4]</td><td>2NRTIs + DTG[2] In consultation with an expert, ensure that at least 1 NRTI is active.[3]</td><td>Continue current regimen and address adherence.</td><td>2NRTIs + DTG In consultation with an expert, ensure that at least 1 NRTI is active.[3]</td><td>Refer to Third-Line Committee</td><td>2 NRTIs + DTG. In consultation with an expert, ensure that at least 1 NRTI is active. [3]</td><td>Refer to Third-Line Committee.</td></tr>
<tr><td>If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r.</td><td></td><td>If NRTI activity cannot be confirmed, expert will recommend 2 NRTIs + PI/r. Adherence must be addressed.</td><td></td><td>If NRTI activity cannot be confirmed, refer to Third-Line Committee.</td><td></td></tr>
</table>

1. Always check hepatitis B status before stopping TDF. If 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. Prior to DTG initiation, all women and adolescent girls of childbearing potential must be appropriately counseled on the potential risk of neural tube defects with DTG use around conception time.
3. From the DAWNING study, DTG was shown to achieve viral suppression when used in combination on with two NRTIs, at least one of which was fully active. (Aboud, M et al., IAS Oral abstract, 2017). It is as yet unknown if DTG will work if combined with two NRTIs, neither of which are fully active.
4. In the EARNEST study, LPV/r was shown to be effective even if combined with two NRTIs that are known to have genotypic resistance (Paton, et al., N Engl J Med, 2014). For this reason, AZT is omitted from LPV/r-containing regimens when TDF is continued due to HBV co-infection. Resistant NRTIs may be recycled with an active PI if no other feasible options are available.
5. Resistance testing in clients failing DTG may be authorised by an expert on a case-by-case basis.

Third-line

Application forms for third-line antiretroviral therapy can be access at the following link:
http://www.health.gov.za/index.php/affordable-medicines/category/524-third-line-antiretrovirals

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 daily-dose regimens.

<table>
<tr><th>Weight (kg)</th><th colspan="2">Abacavir (ABC)</th><th colspan="2">Lamivudine (3TC)</th><th>Abacavir + Lamivudine (ABC + 3TC</th><th>Dolutegravir (DTG)</th><th>Dolutegravir when on rifampicin</th></tr>
<tr><td>Target dose</td><td colspan="2">8 mg/kg TWICE daily
OR
≥ 10 kg:
16 mg/kg ONCE daily</td><td colspan="2">4 mg/kg TWICE daily
OR
≥ 10 kg:
8 mg/kg ONCE daily</td><td>As for individual medications ONCE daily</td><td>By weight band ONCE daily</td><td>By weight band TWICE daily</td></tr>
<tr><td>Available formulations</td><td colspan="2">Sol. 20 mg/mL
Tabs 60 mg (scored, dispersible),
300 mg (not scored),</td><td colspan="2">Sol. 10 mg/mL
Tabs 150 mg (scored),</td><td>Dispersible tablets: 120/60 mg DT
Tablet: 600/300 mg</td><td>Tabs 50 mg (not scored) TDF/3TC/DTG 300/300/50 mg</td><td>Tabs 50 mg</td></tr>
<tr><td></td><td colspan="7">Currently available tablet formulations of abacavir (except 60 mg), dolutegravir, LPV/r and AZT must be swallowed whole and not chewed, divided or crushed.</td></tr>
<tr><td></td><td colspan="7">< 3 kg: See section 9.1.2: The HIV infected neonate (< 1 month of age).</td></tr>
<tr><td>3–4.9</td><td colspan="2">2 mL 12 hourly</td><td colspan="2">2 mL 12 hourly</td><td rowspan="2">1 x 120/60 mg DT daily</td><td rowspan="5">Avoid using when < 20 kg</td><td rowspan="5">Avoid using when < 20 kg</td></tr>
<tr><td>5–5.9</td><td colspan="2" rowspan="2">3 mL 12 hourly</td><td colspan="2" rowspan="2">3 mL 12 hourly</td></tr>
<tr><td>6-6.9</td><td rowspan="2">1.5 x 120/60 mg DT daily</td></tr>
<tr><td rowspan="2">7–9.9</td><td colspan="2">4 mL 12 hourly</td><td colspan="2">4 mL 12 hourly</td></tr>
<tr><td colspan="2">Choose only one option:</td><td colspan="2">Choose only one option:</td></tr>
<tr><td>10–13.9</td><td>6 mL
OR
2 x 60 mg tabs 12 hourly</td><td>12 mL
OR
4 x 60 mg tabs daily</td><td>6 mL 12 hourly</td><td>12 mL daily</td><td>2 x 120/60 mg DT daily</td></tr>
</table>

<table>
<tr><th rowspan="2">Weight (kg)</th><th colspan="2" rowspan="2">Abacavir (ABC)</th><th colspan="2" rowspan="2">Lamivudine (3TC)</th><th rowspan="2">Abacavir + Lamivudine (ABC + 3TC</th><th rowspan="2">Dolutegravir (DTG)</th><th rowspan="2">Dolutegravir when on rifampicin</th></tr>
<tr></tr>
<tr><td></td><td colspan="2">Choose only one option.</td><td colspan="2">Choose only one option.</td><td></td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>14–19.9</td><td>8 mL
OR
2.5 x 60 mg tabs
12 hourly</td><td>1 x 300 mg tab
OR
15 ml daily</td><td>8 mL
OR
½ x 150 mg tab
12 hourly</td><td>15 mL
OR
1 x 150 mg tab daily</td><td>2.5 x 120/60 mg DT daily</td></tr>
<tr><td>20–22.9</td><td rowspan="2">10 mL
12 hourly
OR
3 x 60 mg tabs
12 hourly</td><td>1 x 300 mg tab + 1 x 60 mg tab daily</td><td rowspan="2">15 mL
OR
1 x 150 mg tab
12 hourly</td><td rowspan="2">30 mL
OR
1 x 300 mg tab
OR
2 x 150 mg tabs daily</td><td rowspan="2">3 x 120/60 mg DT daily</td><td rowspan="3">50 mg tab daily</td><td rowspan="3">50 mg tab
12 hourly</td></tr>
<tr><td>23–24.9</td><td>1 x 300 mg tab + 2 x 60 mg tabs daily</td></tr>
<tr><td>25–29.9</td><td rowspan="4">1 x 300 mg tab
12 hourly</td><td rowspan="4">2 x 300 mg tabs daily</td><td rowspan="4">1 x 150 mg tab
12 hourly</td><td rowspan="4">2 x 150 mg tabs daily
OR
1 x 300 mg tab daily</td><td rowspan="4">1 x ABC/3TC 600/300 mg tab daily</td></tr>
<tr><td>30–34.9</td></tr>
<tr><td>35–39.9</td></tr>
<tr><td>> 40</td><td>50 mg tab daily
OR
1 x TDF/3TC/DTG 300/300/50 mg tab daily</td><td>50 mg tab 12 hourly
OR
1 x TDF/3TC/DTG 300/300/50 mg tab daily
+ 50 mg
12 hours after TLD dose</td></tr>
</table>

Weight (kg)	Lopinavir/ritonavir (LPV/r)	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/r **TWICE daily**	LPV/r std dose + super-boosting with ritonavir (RTV) powder **TWICE daily** (≥ 0.75 x LPV dose 12 hourly)	Double-dose LPV/r tabs ONLY if able to swallow whole LPV/r tabs **TWICE daily**	By weight band **ONCE daily**	By weight band **ONCE daily**	180–240 mg/m^2/dose **TWICE daily**
Available formula–tions	Sol. 80/20 mg/mL Pellets 40/10 mg Adult Tabs 200/50 mg, Paed Tabs 100/25 mg	Oral powder 100 mg/packet	Adult tabs 200/50 mg, Paed tabs 100/25 mg	ATV caps 150, 200 mg: RTV tabs 100 mg	Caps 50, 200 mg Tabs 50, 200, 600 mg (not scored)	Sol. 10 mg/mL Caps 100 mg Tabs 300 mg (not scored), AZT/3TC 300/150 mg
Currently available tablet formulations of AZT must be swallowed whole and not chewed, divided or crushed.						
< 3 kg: See section 9.1.2: The HIV infected neonate (< 1 month of age).						
3–4.9	*1 mL 12 hourly **OR** 2 capsules (pellets) 12 hourly	100 mg (1 packet) 12 hourly	Do not use double-dose LPV/r tabs	Avoid ATV capsules when < 15 kg or < 6 years	Avoid using when < 10 kg or < 3 years	6 mL 12 hourly
5–5.9	*1.5 mL 12 hourly **OR** 2 capsules (pellets) 12 hourly					

<table>
<tr><th>Weight (kg)</th><th>Lopinavir/ritonavir (LPV/r)</th><th colspan="2">Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin)
Choose one of the 2 options below as appropriate</th><th>Atazanavir (ATV) + ritonavir (RTV)</th><th>Efavirenz (EFV)</th><th>Zidovudine (AZT)</th></tr>
<tr><td>6–6.9</td><td rowspan="3">*1.5 mL 12 hourly
OR
3 capsules (pellets)
12 hourly</td><td rowspan="3"></td><td rowspan="3"></td><td rowspan="6"></td><td rowspan="3"></td><td>9 mL 12 hourly</td></tr>
<tr><td>7–7.9</td><td rowspan="3">12 mL
OR
1 cap
12 hourly</td></tr>
<tr><td>8–9.9</td></tr>
<tr><td>10–10.9</td><td rowspan="2">2 mL 12 hourly
OR
4 capsules (pellets)
12 hourly</td><td rowspan="2"></td><td rowspan="2">3 x 100/25 mg tabs 12 hourly</td><td rowspan="2">1 x 200 mg caps/tabs at night</td></tr>
<tr><td>11–13.9</td></tr>
<tr><td>14–14.9</td><td rowspan="3">2.5 mL 12 hourly
OR
5 capsules (pellets)
12 hourly
OR
2 x 100/25 mg paed tabs
12 hourly
OR
1 x 200/50 mg adult tab
12 hourly</td><td rowspan="4">200 mg
(2 packets)
12 hourly</td><td rowspan="4">4 x 100/25 mg tabs 12 hourly
OR
2 x 200/50 mg tabs 12 hourly</td><td rowspan="3">1 x 200 mg cap/tab
+ 2 x 50 mg caps/tabs at night</td><td rowspan="3">15 mL 12 hourly
OR
2 caps morning
1 cap evening</td></tr>
<tr><td>15-16.9</td><td rowspan="2">ATV 1 x 200 mg cap daily +
RTV 1 x 100 mg tab daily</td></tr>
<tr><td>17-19.9</td></tr>
<tr><td>20–24.9</td><td>3 mL 12 hourly
OR
6 capsules (pellets)
12 hourly
OR</td><td>20 mL
OR
2 caps
12 hourly</td></tr>
</table>

<table>
<tr><th>Weight (kg)</th><th>Lopinavir/ritonavir (LPV/r)</th><th colspan="2">Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin)
Choose one of the 2 options below as appropriate</th><th>Atazanavir (ATV) + ritonavir (RTV)</th><th>Efavirenz (EFV)</th><th>Zidovudine (AZT)</th></tr>
<tr><td></td><td>2 x 100/25 mg paed tabs
12 hourly
OR
1 x 200/50 mg adult tab
12 hourly</td><td></td><td></td><td rowspan="3"></td><td></td><td></td></tr>
<tr><td>25–29.9</td><td>3.5 mL 12 hourly
OR
7 capsules (pellets)
12 hourly
OR
3 x 100/25 mg paed tabs
12 hourly</td><td rowspan="4">300 mg
(3 packets)
12 hourly</td><td>6 x 100/25 mg tabs 12 hourly
OR
3 x 200/50 mg tabs 12 hourly</td><td rowspan="2">2 x 200 mg caps/tabs at night</td><td rowspan="4">1 tab 12 hourly
OR
1 x AZT/3TC 300/150 mg tab 12 hourly</td></tr>
<tr><td>30–34.9</td><td rowspan="3">5 mL 12 hourly
OR
10 capsules (pellets)
12 hourly
OR
4 x 100/25 mg paed tabs
12 hourly
OR
2 x 200/50 mg adult tabs
12 hourly</td><td rowspan="3">4 x 200/50 mg tabs 12 hourly
OR
8 x 100/25 mg tabs 12 hourly</td></tr>
<tr><td>35–39.9</td><td rowspan="2">ATV 2 x 150 mg caps daily
+
RTV
1 x 100 mg tab daily</td><td>2 x 200 mg caps/tabs at night</td></tr>
<tr><td>≥ 40</td><td>600 mg tab at night</td></tr>
</table>

*Avoid LPV/r solution in any full term infant < 14 days of age and any preterm infant < 14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.

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 » Weight gain. » Potential teratogenic – Neural tube defects (see recommendations regarding counselling).
Lamivudine (3TC)	Room temperature	» Uncommon
Abacavir (ABC)	Room temperature	» Abacavir Hypersensitivity Reaction: > usually occurs in 1st 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. » **Do not continue or re-challenge with abacavir.**
Specific information on ARVs		
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)		
	Storage	**Adverse effects**
Nevirapine (NVP)	Room temperature	» Skin rash usually occurs in 1st 6 weeks. » Do not increase dosage until rash resolves. » Beware of liver toxicity.
Efavirenz (EFV)		» 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)		» Bitter taste
Lopinavir/ ritonavir (LPV/r)	Use tablets whole, without crushing, halving, biting or chewing.	» Nausea » Vomiting » Diarrhoea

Important side effects of ARVs
(*Consult an expert before stopping ART)

	Continue ART with careful monitoring.	**Consult expert and/or stop treatment.**
Lactic acidosis	» lactate 2–5 mmol/L with no signs or symptoms	» lactate > 5 mmol/L, or » with signs or symptoms or acidosis
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
Increase 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 a medicine from the first-line regimen to one from the second-line regimen 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 undetectable or if the change is made in the first six 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.

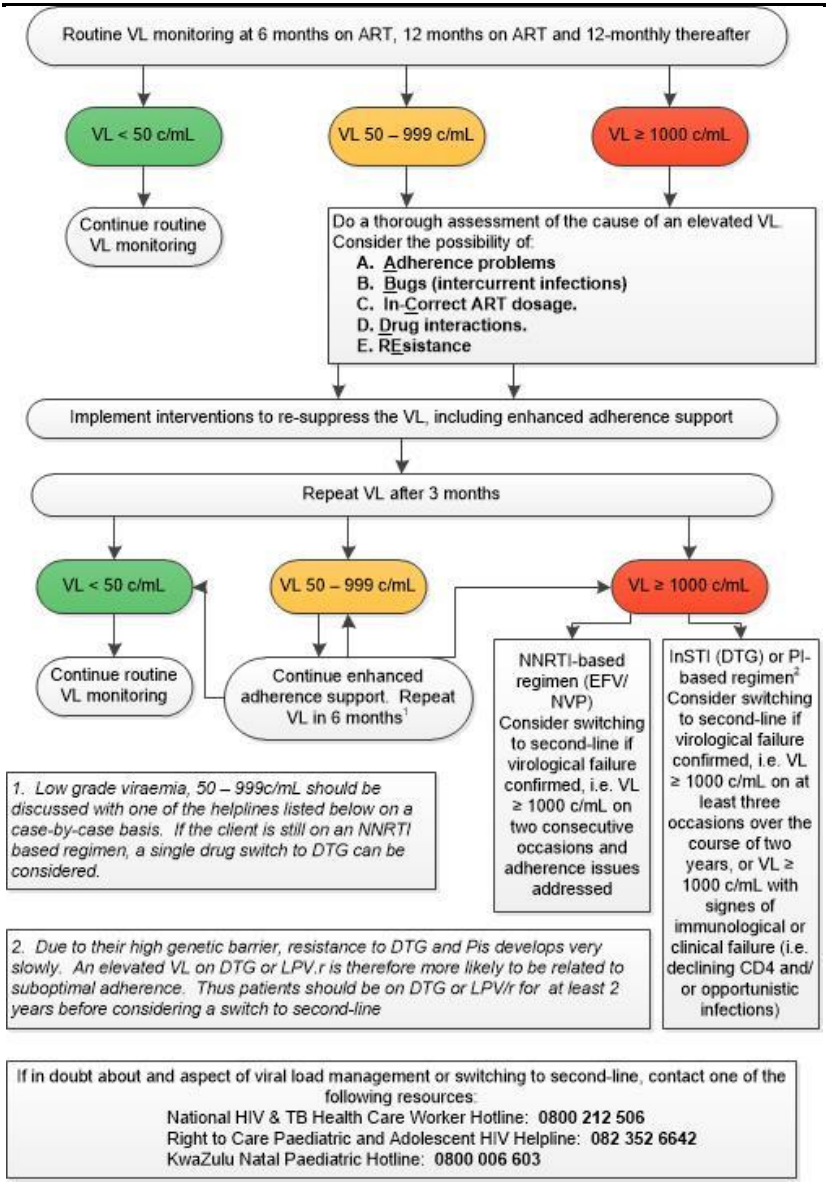
Treatment failure

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 optimal dosage over a four-month period. Treatment failure is defined primarily by viral loads, as waiting for clinical or immunological failure enhances the chances of increasing viral resistance to other available anti-retroviral agents.

The most common cause of failure of first (and subsequent) line therapy is poor adherence. There is no point in changing to second-line therapy before adherence has been addressed.

WHO clinical staging of HIV and AIDS for infants and children
https://www.who.int/hiv/pub/guidelines/arv2013/annexes/WHO_CG_annex_1.pdf



*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 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 (sputums, 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 a close contact with an infectious pulmonary TB case (sputum microscopy smear-positive, culture-positive or *M tuberculosis* PCR test positive), or who are newly found to have a positive TB-lam 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 expert opinion. See Chapter 10: Tuberculosis, section 10.2: Tuberculosis, pulmonary.

TB treatment

If the child is not yet on ART:

» Commence TB treatment first. Follow with ART, usually after 2–4 weeks. In children with TB meningitis, start ART at 4 weeks regardless of CD4 count to avoid IRIS.
» Check ALT before commencing ART. If the ALT is raised, discuss this with an expert as it may not be an absolute contraindication to treatment.
» Assess the child for possible disseminated TB disease.
» Be aware of the possibility of Immune Reconstitution Inflammatory Syndrome (IRIS).

If the child is already on ART:

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

If the child needs to take concomitant ART and rifampicin-containing treatment:

» Dolutegravir: use dolutegravir twice daily.
» Efavirenz: use the normal recommended dosage as per dosing table.
» Abacavir and lamivudine: no adjustment of dosages.
» Lopinavir/ritonavir: refer to dosage table for the ritonavir boosting doses.
» Avoid using double-dose lopinavir/ritonavir solution in young children. 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 an improvement in the immune system 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 2 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 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

For testing, treatment and disclosure, the current acts and regulations should be followed.

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 disclosure is often managed by skilled counsellors. Determine what the adolescent already knows and discuss with the caregiver about who should disclose and where.

Dosage of ARVs

In children over the age of 10 years and over 35 kg use adult dosage regimens – consult ART guidelines[9].

Transition from paediatric ART regimens to adolescent/adult regimens:

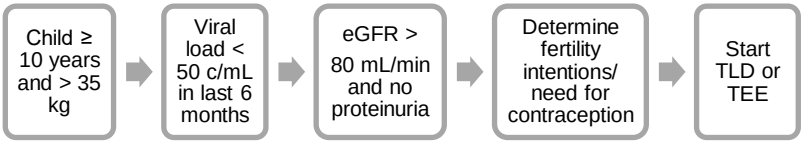
» Adolescents with an undetectable VL (< 50 copies/mL) and no side effects on ABC + 3TC + EFV/DTG can remain on the same regimen until the patient becomes eligible for the TDF + 3TC + DTG (TLD FDC) at 10 years of age and weighing ≥ 35 kg.

» When an adolescent with an undetectable viral load (taken within the last 8 weeks) reaches 10 years of age and is ≥ 35 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, then the patient can be switched to the FDC (TDF + FTC + EFV).

  > 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



If the HIV VL is between 50–1000 copies/mL, consult an expert for advice. If the HIV VL is > 1000 copies/mL, exclude non-adherence then treat as virological failure.

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[10,11]

- 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. 2019 Antiretroviral Therapy Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates. October 2019

[2] South African National Department of Health. Guideline for the Prevention of Mother to Child Transmission of Communicable Infections. November 2019.

[3] Nielsen-Saines K, et. al. Three Postpartum Antiretroviral Regimens to prevent Intrapartum HIV infection. NEJM. 2012;366:2368-2379.

[4] 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.

[5] 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.

[6] 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.

[7] Mazamderani AH, Technau KG, Hsiao NY, Maritz J, Carmona S, Sherman, GG. Recommendations for the management of indeterminate HIV PCR results within South Africa's early infant diagnosis programme. SAJHIVM. 2016; 17(1), a451.

[8] 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.

[9] South African National Department of Health. National Consolidated Guidelines For The Management Of HIV In Adults, Adolescents, Children And Infants And Prevention Of Mother-To-Child Transmission. National Department of Health. February 2020.

[10] 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.

[11] 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.