CONTRACEPTIVE METHODS

Contraceptive Methods

Method	Key Factors
Male Condom **Female Condom**	• 85-98% effective as contraceptive method when used consistently and correctly • Overall 80% effective in preventing STIs, including HIV • Does not affect breastfeeding or interact with medications • Must counsel regarding correct use • Promote and provide access to emergency contraception
	Condom use should always be encouraged as dual method use to maximize HIV and pregnancy protection
Low-dose Combined oral contraceptives (COCs)	• Low-dose COCs are those with ≤ 35 ug synthetic oestrogen ethinyl estradiol • 92-99.7% effective as contraceptive, primarily by preventing ovulation • Measure blood pressure prior to initiation, when possible • May initiate at any time, if not pregnant or breastfeeding. No restrictions on use from menarche to age 40. After age 40 generally can use, but more • careful follow-up may be required • If breastfeeding, or at 6 months postpartum or after she stops breastfeeding—whichever comes first • **Drug interactions, including with some antiretrovirals** *Note: All women on COCs ≥35ug ethinyl estradiol should be switched to low –dose COC*
Progestin-only Pills	• POPs are appropriate for breastfeeding women and are a useful alternative for women who experience oestrogen-related side effects with COCs, or have health conditions that may preclude safe use of • COCs. • As commonly used, 90-92% effective; ≥99% effective if breastfeeding • Primarily thickens cervical mucus and so prevents sperm penetration (after 2 days of use). Also inhibits ovulation in 60% of cycles.

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Method	Key Factors
Progestin-only Injectables (DMPA and NET-EN)	• Injectables: 94% effective as commonly used; if return for re-injection on time 99.7% effective as contraceptive • Concerns regarding bone mineral density in women < 18 years and > 45 years • Not protective against STIs, including HIV. Recent studies suggest they may increase the risk of HIV acquisition (specifically DMPA). While awaiting additional research, emphasise importance and proper condom use in conjunction with hormonal and non-hormonal contraceptives to prevent HIV. • Alternatives, such as lower dose hormonal contraceptives, and non-hormonal options, such as Cu IUDs, need to be explored with the client. Weigh risk of possible HIV against benefits in preventing pregnancy.
Implant	• Implants: Almost 100% effective, remain in place for 3-5 years • **NOT recommended for women on Efavirenz, Rifampicin, and certain epilepsy drugs** as it may lower efficacy of implant; always cover with another method in women who already on implant device and on above drugs. • Not protective against STIs and HIV
Intrauterine Contraception non-hormonal (Copper - CuIUD)	• Highly effective, long-acting and reversible method • Approved for use up to 10 years (copper) • 99.2-99.4% effective • No age restrictions • Does not affect breastfeeding, intercourse or have hormonal side effects • Do not protect against STIs, including HIV and dual method with consistent condom use should be recommended
Levonorgestrel releasing intrauterine system (LNG-IUS, Mirena)	• Releases a constant, small amount of pregestogen directly into the uterine cavity. • Failure rate of 0.2% and continuation rate of 80% at one year, as effective as male and more effective than female sterilisation • Thickens cervical mucous and suppresses endometrial development • This method is currently only available to clients in private sector and some secondary/tertiary institutions

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Method	Key Factors
Emergency Contraception	• Use at any time during menstrual cycle within 5 days (120 hours) following unprotected intercourse • ECPs – POPs 58-95% effective, COCs 31-77% effective (effectiveness depends on how soon initiated following unprotected intercourse) • Cu IUD – fails in only < 0.1% of cases. Insert under antibiotic cover (to prevent STIs) and remove during the next menstrual period **Risk of infection is higher than risk for pregnancy. Screen for STIs and consider post-exposure prophylaxis for HIV*
Sterilisation	• Should not be co-erced or performed without consent • Permanent contraceptive methods • Female sterilisation – 99.5-99.8% effective year one, 98.2% over 10 years. • Male sterilisation (vasectomy) – 99.8% effective (use back-up method for 3 months following as may continue to have ejaculate for 3 months)
Lactational Amenorrhoea Method	• Breastfeeding as temporary method of contraception, 98-99% effective if amenorrhoeic and fully breastfeeding during first 6 months after childbirth
Fertility Awareness-Based Methods	• Based on identification of natural signs and symptoms of fertile and infertile phases of menstrual cycle. Requires abstinence or condom use during the fertile phase of each cycle. • Depends on a woman's ability to identify her fertile window, as well as both partners' motivation and discipline to practise abstinence (or use condoms) when required. 95–97% effective during first year of consistent and correct use but only 75% effective as commonly used
Withdrawal Method	• Withdrawing penis from vagina and external genitalia prior to ejaculation • 73% during first year, 96% if consistent and correctly used

Sources: South Africa NDOH. Contraception Clinical Guidelines. 2012. Morrison J et al. Hormonal contraception and HIV acquisition: reanalysis using marginal structural modelling. AIDS, 2010, 24(11). Heffron R et al. Use of hormonal contraceptives and

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risk of HIV-1 transmission: a prospective cohort study. Lancet Infectious Diseases, 2011, doi: 10.1016/S1473-3099(11)70247-X (accessed 11 November 2011). WHO. Hormonal contraception and HIV. Technical Statement. Geneva: World Health Organization, 2012. South African Clinician's Society. Guideline on Safer Conception in Fertile HIV-Infected Individuals and Couples, June 2011.

DRUG SIDE EFFECT MONITORING

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Side Effects by ARV Class

Protease Inhibitors	Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
Metabolic Disorders • Hepatotoxicities • Hyperglycemia, insulin resistance • Lipid abnormalities • Fat redistribution **Drug Interactions** **GI Intolerance** **Bone Disorders** **CYP450 3A4 Inhibition**	**Nausea** (All) **Headache** (All) **Anaemia** (AZT) **Renal Toxicity** (TDF) **Peripheral neuropathy** (D4T/DDI) **Fat redistribution** (all, except TDF) **Pancreatitis** (DDI > D4T) **Lactic acidosis, fatty liver** • D4T + DDI > D4T > ZDV • Rare with ABC, TDF, 3TC and FTC	**Side effects:** **Rash** (EFV , NVP) **Hepatotoxicity** (NVP) **Dizziness, vivid dreams and other central nervous system** (EFV) **Across the class** • Cross Resistance

Grading of Adverse Events in Adults and Children

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Haematology				
Haemoglobin Infant 1-21 days	12.0-13.0 g/dL	10.0-11.9 g/dL	9.0-9.9g/dL	< 9.0g/dL
Haemoglobin Infant 22-35 days	9.5-10.5g/dL	8.0-9.4 g/dL	7.0-7.9g/dL	< 7.0g/dL
Haemoglobin Infant 36-56 days	8.5-9.4g/dL	7.0-8.4g/dL	6.0-6.9g/dL	< 6.0g/dL
Hb ≥ 57 days (HIV-positive only)	8.5-10.0g/dL	7.5-8.4g/dL	6.5-7.4g/dL	< 6.5g/dL
Absolute neutrophil count – Infant 1 day	4.0-5.0x109/l	3.0-3.9x109/l	1.5-2.9x 109/l	< 1.5 x 109/l
Absolute neutrophil count – Infant 2-7days	1.25-1.5x109/l	1.0-1.24x109/l	0.75-0.99x109/l	< 0.75x109/l
Absolute neutrophil count – Children ≥ 7 days	1.0-1.3 x109/l	0.75-0.9 x109/l	0.5-0.75 x109/l	< 0.5 x109/l

Continued

Grading of Adverse Events in Adults and Children

Continued

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Haematology				
Platelets (cells/ µl)	100,000–124,999 /mm^3	50,000–99,999 /mm^3	25,000–49,999 /mm^3	< 25,000/mm^3 or bleeding
Gastro-intestinal				
Bilirubin	1.1–1.5 x ULN	1.6–2.5 x ULN	2.6 – 5.0 x ULN	> 5 x ULN
AST	1.25–2.5 x ULN	2.6– 5.0 x ULN	5.1– 10.0 x ULN	> 10.0 x ULN
ALT	1.25–2.5 x ULN	2.6– 5.0 x ULN	5.1– 10.0 x ULN	> 10.0 x ULN
γGT	1.1 – 4.9 x ULN	5.0 – 9.9 x ULN	10.0 – 15.0 x ULN	> 15.0 x ULN
Pancreatic Amylase	1.1–1.5 x ULN	1.6 – 2.0 x ULN	2.1 –5.0 x ULN	> 5.0 x ULN
Diarrhoea Adult and paediatric ≥ 1 year	Transient or intermittent episodes of unformed stools **OR** Increase of ≤3 stools over baseline per 24-hour period	Persistent episodes of unformed to watery stools **OR** Increase of 4-6 stools over baseline per 24-hour period	Bloody diarrhoea **OR** Increase of ≥7 stools per 24-hour period **OR** IV fluid replacement indicated	Life-threatening consequences (e.g., hypotensive shock)

Continued

Grading of Adverse Events in Adults and Children

Continued

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Gastro-intestinal				
Diarrhoea Paediatric < 1year	Liquid stools (more unformed than usual) but usual number of stools	Liquid stools with increased number of stools **OR** Mild dehydration	Liquid stools with moderate dehydration	Liquid stools resulting in severe dehydration with aggressive rehydration indicated **OR** Hypotensive shock
Constipation	NA	Persistent constipation requiring regular use of dietary modifications, laxatives, or enemas	Obstipation with manual evacuation indicated	Life-threatening consequences (e.g., obstruction)
Nausea	Transient (< 24 hours) or intermittent nausea with no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24-48 hours	Persistent nausea resulting in minimal oral intake for > 48 hours **OR** Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting resulting in orthostatic hypotension **OR** Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)

Continued

Grading of Adverse Events in Adults and Children

Continued

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Allergic / Dermatological				
Acute systemic allergic reaction	Localised urticarial (wheals) with no medical intervention indicated	Localised urticaria with medical intervention indicated **OR** Mild angioedema with no medical intervention indicated	Generalised urticaria OR Angioedema with medical intervention indicated **OR** Symptomatic mild bronchospasm	Acute anaphylaxis **OR** Life threatening bronchospasm **OR** Laryngeal oedema
Cutaneous reactionskin rash*	Localised macular rash	Diffuse maculopapular rash **OR** Morbilliform rash **OR** Target lesions	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae **OR** Superficial ulcerations of mucous membrane limited to one site	Extensive/generalized bullous lesions **OR** Stevens-Johnson syndrome **OR** laceration of mucous membrane involving two or more distinct mucosal sites **OR** Toxic Epidermal Necrolysis (TEN)

Continued

Grading of Adverse Events in Adults and Children

Continued

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Nervous system				
Developmental delay– Paediatric <1 Years	Mild developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Moderate developmental delay, motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Severe developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Developmental regression, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting
Neuromuscular weakness(including myopathy and neuropathy)	Asymptomatic with decreased strength on exam **OR** Minimal muscle weakness causing no or minimal interference with usual social and functional activities	Muscle weakness causing greater than minimal interference with usual social and functional activities	Muscle weakness causing inability to perform usual social and functional activities	Disabling muscle weakness causing inability to perform basic self-care functions **OR** Respiratory muscle weakness impairing ventilation

Continued

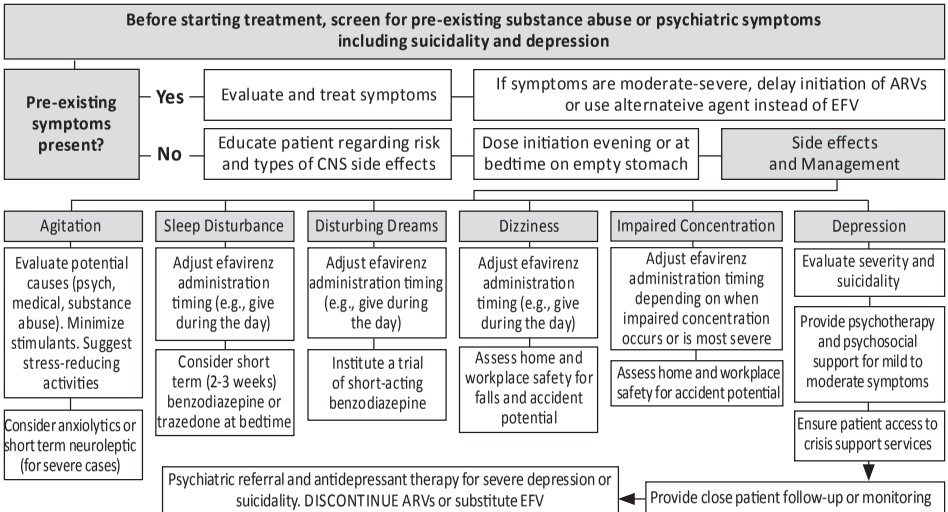
Grading of Adverse Events in Adults and Children

Continued

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Nervous system				
Neurosensory alteration (including paraesthesia and painful neuropathy)	Asymptomatic with sensory alteration on exam or minimal paraesthesia causing no or minimal interference with usual social and functional activities	Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities	Sensory alteration causing inability to perform usual social and functional activities	Disabling sensory alteration or paraesthesia causing inability to perform basic selfcare functions
Other				
Clinical symptoms not otherwise specified above	No therapy, monitor condition	May require minimal intervention and monitoring	Requires medical care or possible hospitalisation	Requires active medical intervention, hospitalisation or hospice care

Source: National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults, December 2014.

Management of Efavirnez-related Central Nervous System Side Effects

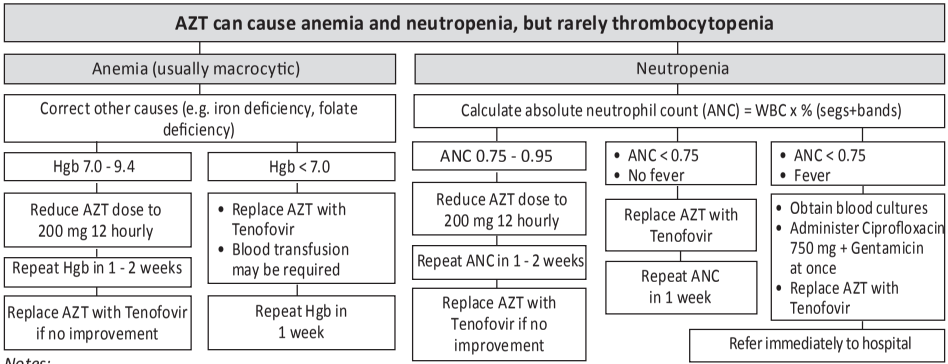


Notes:

1. If a switch from efavirenz to nevirapine is made, the lead-in dose is not required and nevirapine should be started at a dose of 200mg bd

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

AZT-Related Hematologic Toxicity

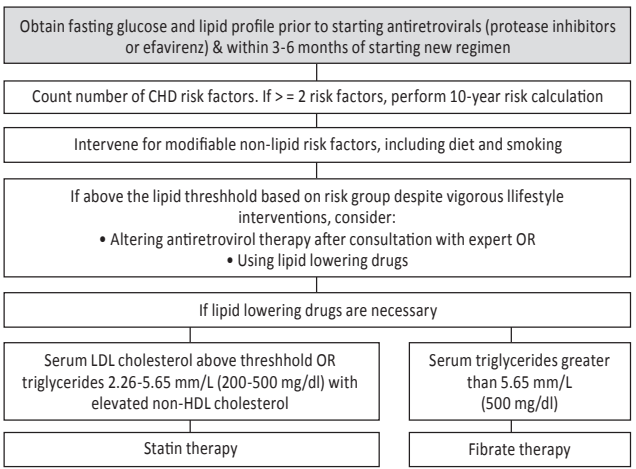


Notes:

1. *Systematic evaluation of anaemia is based on MCV (microcytic, normocytic, macrocytic), whether bone marrow response is appropriate (high reticulocyte count), whether all cell lines are involved (pancytopenia) or not.*
2. *AZT causes a hypoproliferative macrocytic anaemia. Another cause of severe hypoprolifertive anaemia in HIV patients is Parvovirus induced pure red cell aplasia.*
3. *If anaemia and thrombocytopenia are present, consider the possibility of thrombotic thrombocytopenic purpura (TTP) and examine blood smear for schistocytes.*
4. *Reference: South Africa. National Department of Health. CLINICAL GUIDELINES FOR THE MANAGEMENT OF HIV & AIDS IN HEALTH FACILITIES (2008). Section 3.8*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Dyslipidemia Management

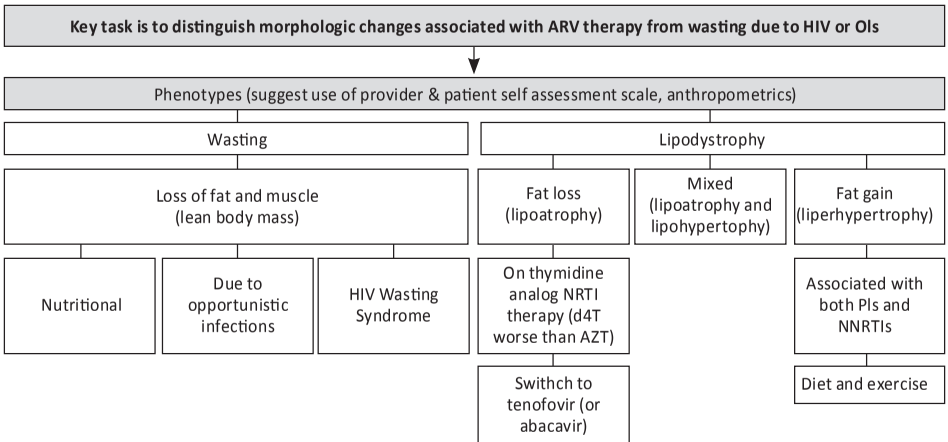


Notes:

1. *Treat patients with hypertriglyceridaemia where the triglyceride level is > 10 mmol/L medical therapy with a fibrate (e.g. Bezafibrate 400 mg daily after food). "The main risk associated with hypertriglyceridaemia is pancreatitis (usually when level is > 15 mmol/L).*
2. *Major risk factors (exclusive of LDL cholesterol) that modify LDL goals are: cigarette smoking, hypertension (BP > = 140/90 or on antihypertensive medication), low HDL cholesterol (< 1 mmol/L or <40 mg/dl), family history of premature CHD (CHD in male first degree relative < 55 years; Diabetes CHD in female first degree relative < 65 years), age (men > = 45 years; woment > = 55 years). Diabetes is regarded as a CHD equivalent.*
3. *10-year cardiovascular risk assessment tools (Framingham) available at: http://cvrisk.mvm.ed.ac.uk/calculator/calc.asp (using mmol/L units) and http://hp2010.nhlbihin.net/atpiii/calculator.asp (using mg/dL units)*
4. *Treat patients with a statin if their Framingham risk for MI is calculated to be 20% over 10 years.*
5. *Simvastatin and most other statins are contra-indicated for use with PIs because of drug interactions. However, Pravastatin and low dose Atorvastatin are safe.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Wasting and Lipodystrophy Management



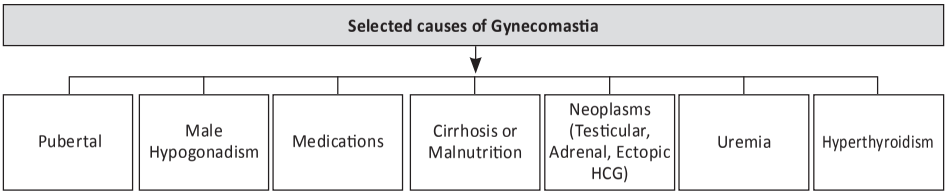
Notes:

1. Increase in triglycerides has been shown to be a predictor of lipodystrophy in a number of studies.

2. Increased lactic acid levels may be associated with a higher risk of lipoatrophy.

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Gynecomastia

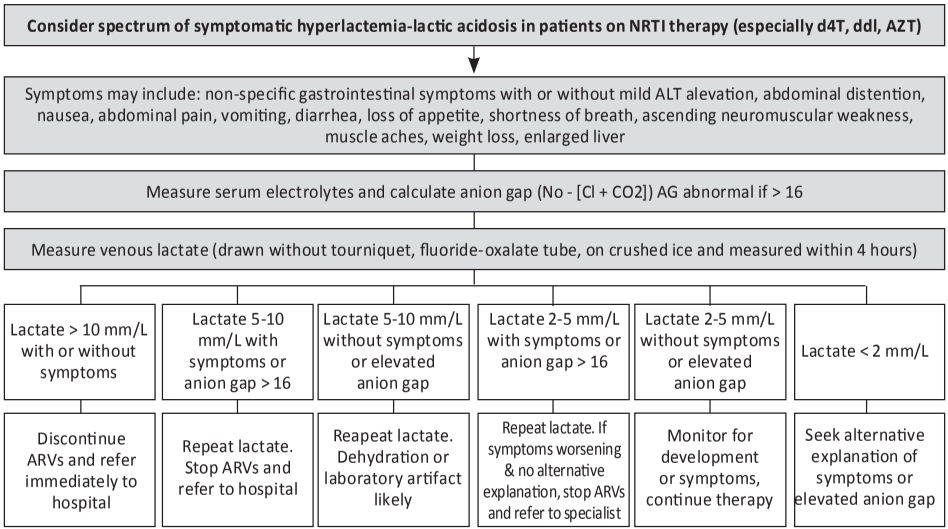


Notes:

1. *Efavirenz and ddI have been associated with developement of gynecomastia. In most cases it resolves spontaneously over 1-2 years. Switch drugs if its effects are severe (e.g. psychological distress). Neviropine could be an option (monitor hepatotoxicity in regard to CD4 levels).*
2. *Many other drugs have been associated with development of gynecomastia. Commonly used ones include: spironolactone, isoniazid, cimetidine, ACE inhibitors, calcium channel blockers, anabolic steriods, estrogens, haloperidol, phenothiazines, tricyclic antidepressants, phenytoin, metoclopramide.*
3. *Evaluation of hormonal causes would include (when available) measurement of: testosterone, LH, HCG estradiol, and TSH. Generally refer to a specialist when hormonal causes are suspected.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Hyperlactatemia and Lactic Acidosis due to NRTI Therapy



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Hyperlactatemia and Lactic Acidosis due to NRTI Therapy

Continued

Notes:

1. *In patients with mild hyperlactataemia and minimal symptoms (lactate 2.5-5 and no metabolic acidosis - standard bicarbonate > 20):*
   - *The d4T should be switched to AZT*
   - *The lactate rechecked within 3 days and then weekly until normalized*
   - *Stop ART if the lactate cannot be nonitored in the way described*
   - *Stop ART and follow the guidelines below if symptoms are severe or the lactate continues to rise or symptoms get worse despite the switch*
2. *Patients with moderately sever hyperlactataemia/moderate metabloic acidosis (lactate 5-10 and/or standard bicarbonate 15-20):*
   - *Stop ART and observe as inpatient for 1-2 days*
   - *Give oral vitamins (vitamin BCo 2 tablets bd and thiamine 100 mg bd)*
   - *Hydrate well (orally or IVI)*
   - *Exclude sepsis*
   - *Exclude OIs*
   - *Recheck lactate and discharge for outpatient follow-up if clinically stable*
   - *Recommence ART regimen 1d (Tenofovir, 3TC, EFV) only when lactate and bicarbonate has normalized (this may take months)*
3. *Patients with severe hyperlactataemia (lactate > 10 without metabolic acidosis) or significant lactic acidosis (raised lactate regardless of level and significant metabolic acidosis - standard bicarbonate < 15). The mortality is high in this scenariao (up to 60%). These patients should preferably be managed in a hight care facility as such:*
   - *Stop ART*
   - *IVI Thiamine 100 mg 12 hourly and BCo 1 amp 12 hrly*

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Hyperlactatemia and Lactic Acidosis due to NRTI Therapy

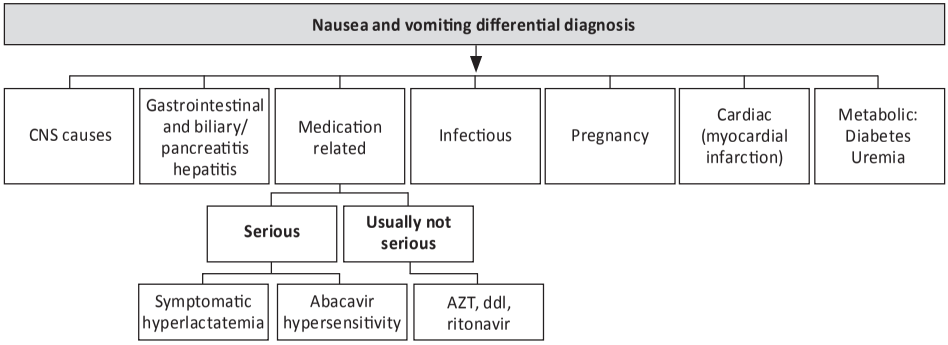
Notes Continued:

- *IVI fluids*
- *Blood culture / urine culture / septic search AND*
- *Broad-spectrum antibiotic (e.g. third-generation cephalosporin or co-amoxyclav). This is important because sepsis may mimic or precipitate NRTI-associated lactic acidosis.*
- *IVI NaHCO3 if profound acidosis*
- *Ventilation if respiratory fatigue occurs*
- *Dialysis*
- *Inotropes AND*
- *Other supportive measures as necessary*
- *Monitor:*
  - *Lactate*
  - *Blood gas*
  - *Lipase*
  - *ALT and*
  - *Alkaline Phosphatase*
- *Recommence ART Regimen 1d (Tenofovir, 3TC, EFV) Lopinavir/Ritonavir (Kaletra) when lactate has significantly decreased and they are clinically improved (this may take weeks to months)*

1. *Neither d4T nor ddI should be used ever again in any patient who has had symptomatic hyperlactataemia/lactic acidosis.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Nausea and Vomiting

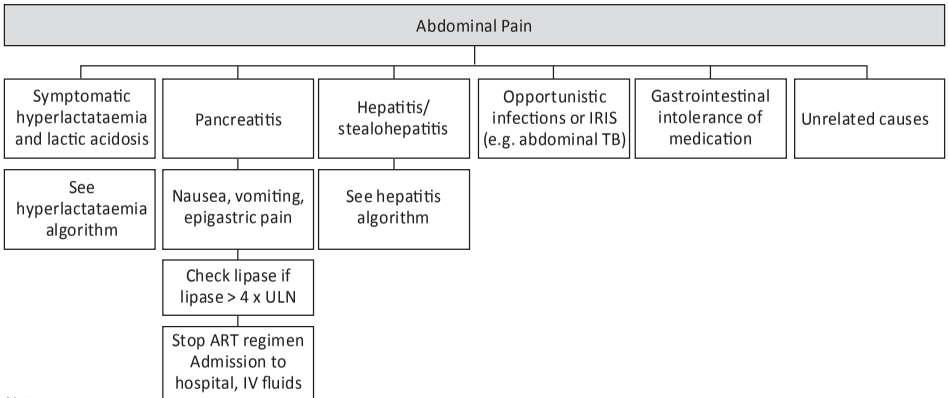


Notes:

1. *Symptomatic hyperlactatemia due to d4T and other NRTIs can present with loss of appetite, nausea and vomiting. See Lactic Acidosis algorithm.*
2. *Abacavir hypersensitivity (HSR) can present with gastrointestinal symptoms. See Abacavir HSR algorithm.*
3. *D4T and ddI can casue pancreatitis, presenting with nausea, vomiting and epigastric pain. See abdominal pain algorithm.*
4. *Actively manage nausea due to antiretroviral medication, or adherence will suffer. The common causative agents are AZT and ddI.*
5. *Administering anti-emetics half an hour before the antiretroviral dose up to 3 times daily may be helpful. If the nausea does not settle, refer to a doctor trained on ART.*
6. *Check for jaundice and take blood for ALT as nausea and vomiting may be the first symptoms of drug-induced hepatitis.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Abdominal Pain

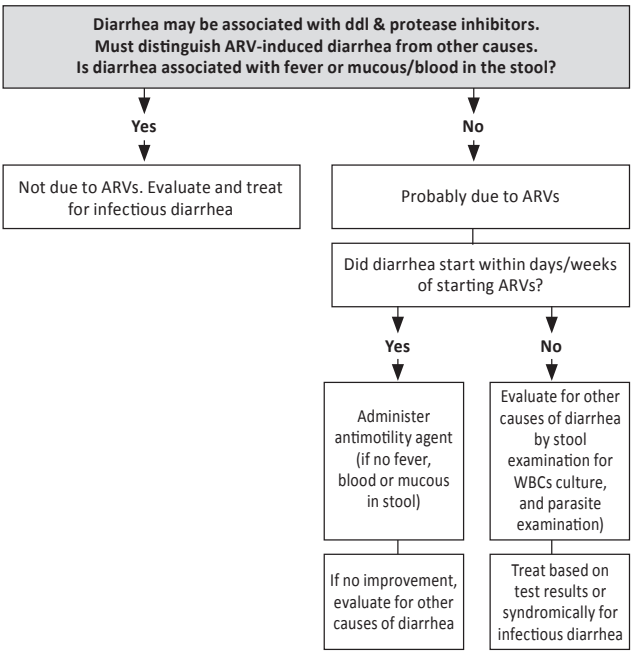


Notes:

1. *Causes of pancreatitis include drug induced (d4T, ddI, 3TC (in children), Kaletra), infections (e.g. CMV) alcoholic pancreatitis, hypertriglyceridemia and biliary pathology (e.g. gallstones).*
2. *NRTI induced pancreatitis may be associated with mitochondrial toxicity. Check lactate after hemodynmically stabilized.*
3. *Unrelated causes include: pregnancy, diabetic ketoacidosis, appendicitis, peptic ulcer disease, pelvic inflammatory disease, and urinary tract infections.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

ARV-Associated Diarrhea Management

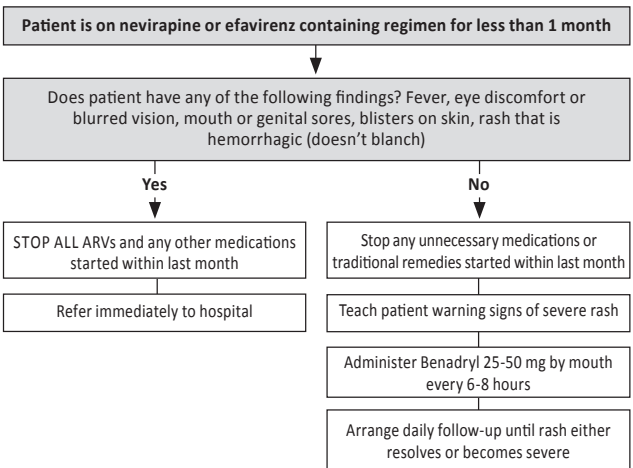


Notes:

1. *For symptomatic treatment of non-inflammatory diarrhea, use Loperamide, oral, 4 mg immediately, followed by 2 mg after each loose stool, up to 16 mg/day for severe diarrhea, OR Codiene syrup/tablets 15-30 mg po 3-5 times a day (as required).*
2. *Ensure hydration with home-made sugar and salt solution: 1/2 level teaspoon of salt and 8 level teaspoons of sugar dissolved in 1 litre of boiled then cooled water.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

ARV Rash Management Flow Chart

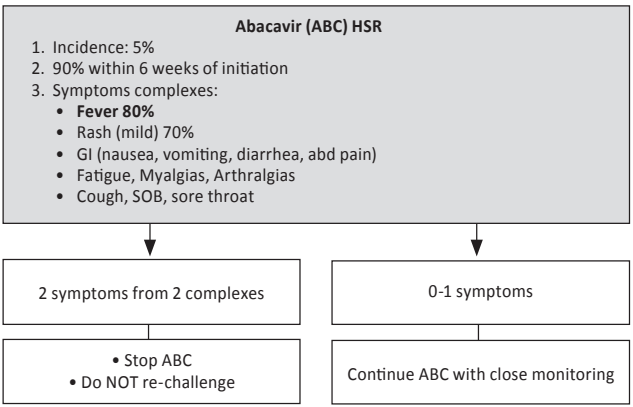


Notes:

1. *Drug rashes are typically associated with nevirapine (and the abacavir hypersensitivity syndrome which is covered separately). Less commonly they are associated with efavirenz and rarely with other antiretrovirals. A number of other drugs used in patients with HIVs (e.g. co-trimoxazole and TB medications) may also result in drug rashes.*
2. *About 15% of patients started on nevirapine will develop a drug rash. This typically occurs in the first 3 months. It typically presents with a morbiliform or maculo-papular eruption but may progress to blistering, desquamation and a Stevens-Johnson syndrome.*
3. *Most nevirapine skin rashes are mild and will settle despite continuing the drug. However, about 7-33% of patients require that nevirapine be stopped.*
4. *Check the following in patients presenting with a nevirapine skin rash: ALT, temperature, ask about systemic symptoms.*
5. *Avoid systemic steroids in HIV patients with Stevens Johnson Syndrome unless there is evidence of adrenal insufficiency.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Abacavir Hypersensitivity Reaction (HSR)



Notes:

1. *Use caution when initiating ABC if Immune Reconstitution Syndrome (IRIS) likely (e.g. recent TB diagnosis) to avoid confusion when fever occurs.*
2. *ABC HSR symptoms usually worsen daily if ABC continued.*
3. *ABC HSR can progress to multi-organ failure and death, especially with re-challenge.*
4. *Rash alone not indicative of ABC HSR.*
5. *If HLA-B*5701 testing available, do not use ABC if positive.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Peripheral Neuropathy

- **Don't start ddl of d4T containing regimen if patient has symptoms of pre-existing neuropathy**
- **If pre-existing neuropathic symptoms, determine causes and treat (nutritional, drug induced e.g. INH diabetes, alcohol)**
- **Neuropathic symptoms due to HIV itself: diagnosis of exclusion**

Symptoms

Peripheral Neuropathy symptoms: Burning, tingling pain of feet, often worse at night. Occasionally manifest by leg cramps

Grade the severity of symptoms and relationship to start d4T and ddl (e.g. visual analog scale 0-10; Brief Neuropathy Screening Tool (BNST))

Pain Mild

- Symptomatic therapy with simple analgesia Amitriptyline 25-75 mg daily
- Vitamin supplementation (B6 and BCo)
- Selected self care modalities

No relief or worsens

- Switch to AZT if not contraindicated
- If AZT contraindicated, switch to Tenofovir

Pain Moderate or Severe (not controlled with NSAIDs, adjuvants, and vitamin supplementation)

- Switch to AZT if not contraindicated
- If AZT contraindicated, switch to Tenofovir
- Palliate pain with more effective adjuvants and opiates

Notes:

1. *Additional adjuvants with same demonstrated efficacy for HIV distal symmetric polyneuropathy include gabapentin and lamotrigine.*
2. *Antiepileptic drugs including phenytoin and carbamazepine are both inducers of the cytochrome P-450 enzyme system and can lower levels of antiretrovirals metabolized by that system (NNRTIs and protease inhibitors) and compromise antiretroviral therapy effectiveness.*
3. *Self-help strategies such as warm baths have been reported in observational studies to palliate HIV-related neuropathic pain.*
4. *Depending on clinical picture, d4T can be switched with Tenofovir. Tenofovir can also be used in place d4T when initiating therapy.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Glucose Intolerance, Dibetes, and Metabolic Syndrome

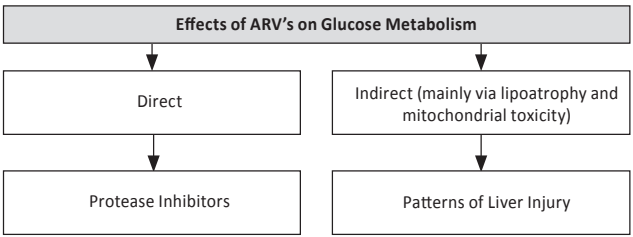
Definitions of Abnormal Glucose Metabolism			
	Fasting mmol/L (mg/dL)	**After OGTT mmol/L (mg/dL)**	Comments
Normal	< 5.5 (<100)	< 7.7 (<140)	Symptoms (poyuria, polydypsia, weightloss + random glucose ≥ 11 mmol/L)
Pre-Diabetes	IFG: 5.5-6.89 (100-125)	7.7-10.99 (140-199)	
Diabetes	≥ 6.9 (≥ 126)	≥ 11 (≥ 200)	
OGTT: Oral Glucose Tolerance Test (75 gm glucose load) IFG: Impaired Fasting Glucose			

Notes:

1. *A diagnosis of Metabolic Syndrome requires the presence of at least 3 of the following componets: impaired glucose tolerance, hypertension, elevated waist circumference or waist-hip ratio, and high triglyceride and/or low high-density lipoprotein cholesterol (HDL-C) levels. Metabolic Syndrome increases risk of diabetes and confers 3-fold increased risk of cardiovascular disease.*
2. *Effects of protease inhibitors (Pls) on glucose metabolism vary by agent. Among the Pls, atazanavir, darunavir, and saquinavir have least deleterious effects on glucose metabolism (not currently available in South African antiretroviral therapy program). Effects of Kaletra appear to be less than Indinavir, which has the greatest impact among the Pls.*
3. *Non-antiretroviral drugs including niacin, corticosteroids, and thiazide diuretics may impair glucose metabolism and therby worsen insulin resistance and diabetes.*
4. *Abacavir has been associated with increased risk of cardiovascular events in recent epidemiological studies.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Effects of ARV's on Glucose Metabolism



Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Tenofovir-Related Nephrotoxicity

Reported Forms of Tenofovir Nephrotoxicity

- Acute renal failure
- Fanconi Syndrome (glyosuria, phosphaturia, aminoaciduria)
- Nephrogenic diabetes insipidus

Antiretroviral Drug, Dosing Category	
Tenofovir	**Dosage**
Usual dosage	300 mg po q.d.
	Dosage for patients with CKD or ESRD
Creatinine clearance ≥ 50 mL/min	No adjustment
Creatinine clearance 30-49 mL/min	300 mg po q48h
Creatinine clearance 10-29 mL/min	300 mg po q72h
Receiving hemodialysis	300 mg po every 7 days[c]
Receiving peritoneal dialysis	Unknown, use with caution

Cockcroft-Gault Equation (Creatinine clearance calculation equation)

$$\text{CrCl} = \frac{(140\text{-age}) \times (\text{IBW in kg}) \times (0.85 \text{ if female})}{\text{Serum Cr in mg/d/} \times 72}$$

Estimated Ideal Body Weight (IBW) in kg: IBW = 50kg (male) or 45kg (female) + 2.3kg for each inch > 5 ft.

In Sa: IBW = 50kg (male) or 45kg (female) + 2.3kg x $\frac{(\text{Actual height in cm} - 152.4\text{cm})}{2.5\text{cm}}$

Continued

Tenofovir-Related Nephrotoxicity

Continued

Notes:

1. *Clinically significant nephrotoxicity in patients with normal underlying renal function is rare.*
2. *Patients receiving tenofovir who have a GFR > 90 mL/min per 1.73 m2, patients receiving other medications eliminated via renal secretion (e.g., adefovir, acyclovir, ganciclovir, or cidofovir), patients with other comorbid diseases (e.g., diabetes or hypertension), or patients receiving ritonavir boosted protease inhibitor regimens should be monitored at least biannually for measurements of renal function, serum phosphorus, and urine analysis for proteinuria and glycosuria.*
3. *Avoid concimittant use of nephrotoxic medications with tenofovir (e.g. aminoglycosides, amphotericin B, foscarnet).*
4. *Dosing of tenofofir should be based on estimated creatinine clearance (CrCl) using the Cockcroft-Gault formula above. The following website can be used to calculate CrCl: http://nephron.com/cgi-bin/CGSI.cgi*
5. *Fanconi Syndrome, a proximal tubular disorder, should be suspected when normoglycemic glycosuria, hypophosphatemia, and proteinuria are persistently present.*

Reference: South Africa. National Department of Health. ANTIRETROVIRAL THERAPY in SOUTH AFRICA: A Pocket Guide on Prevention and Management of Side Effects and Drug Interactions (2009)

Interpreting Blood Results: Alanine Transaminase (ALT)

ALT should be pulled for:
- Alternating nightshift/dayshift workers
- Patients with significant psychiatric/substance abuse/alcohol history

Gender	Normal Range	< 2x ULN	2 - 3x ULN	> 3 x ULN	5x ULN
Female	0-35	< 70	70-105	> 105	175
Male	0-40	< 80	80-120	> 120	200
Nevirapine Use	NVP safe	NVP safe	Avoid NVP	Avoid NVP	Avoid NVP
Referral	No		No	Consider (Phone)	Immediate
Additional Investigations	None		Hep B sAg Full LFT	→ Full Hepatitis Screen → Full LFT → Abdo Sonar → Look for TB → Other drugs?	Full work-up to be done at up-referral site

Continued