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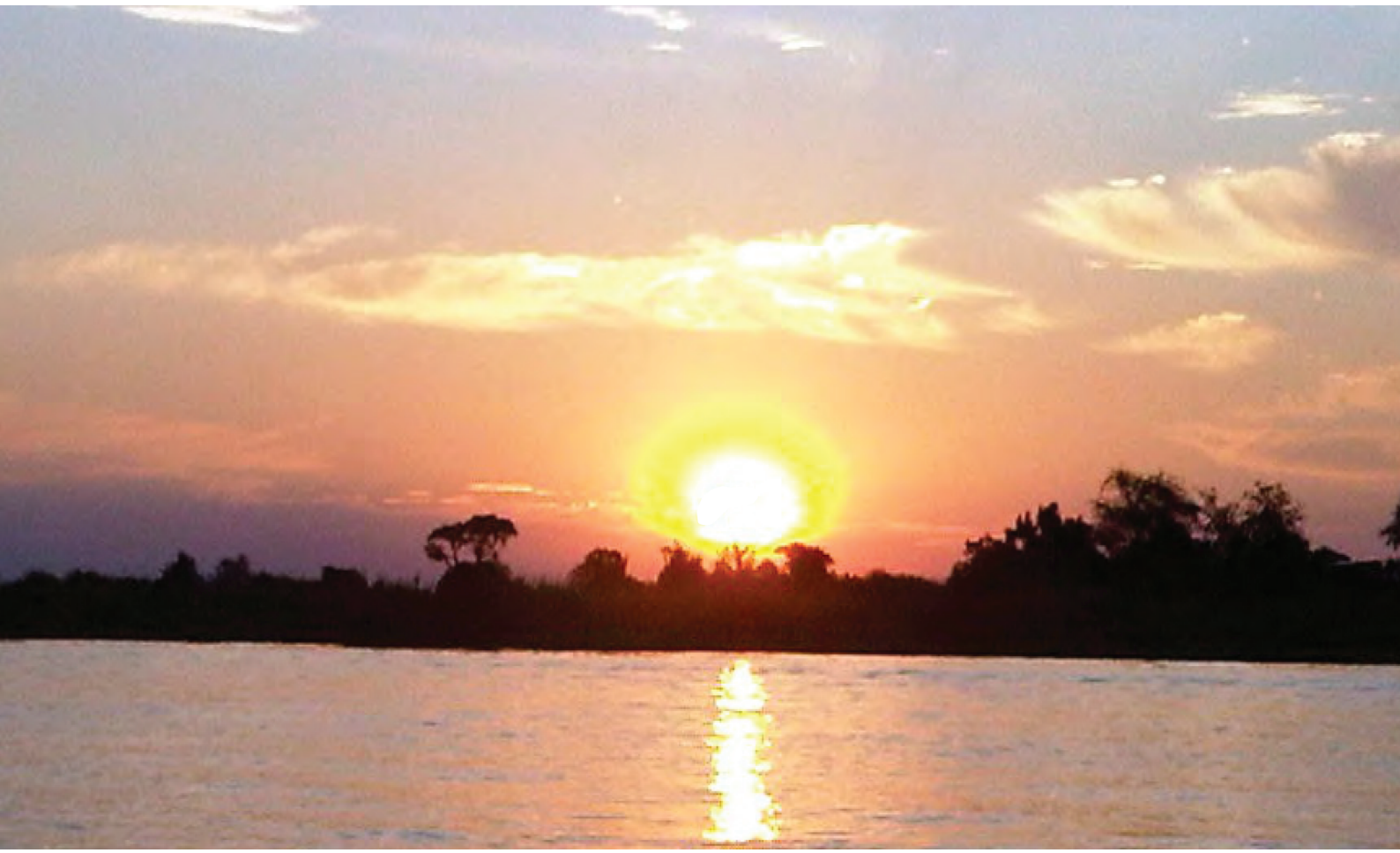


HANDBOOK OF THE BOTSWANA 2016 INTEGRATED HIV CLINICAL CARE GUIDELINES

MINISTRY of HEALTH
REPUBLIC OF BOTSWANA

DEPARTMENT OF HIV/AIDS PREVENTION AND CARE

Masa Antiretroviral Therapy
Lenaneo la Melemo ya go Ritibatsa Mogare wa HIV/AIDS

Treat ALL

PREFACE

2016 will mark an important turning point in the Botswana National HIV Response. The implementation of our New HIV 'Treat All' Strategy promises to take our country forward as we collectively put an end to AIDS. If we all play our part, thousands of lives will be saved from HIV infection and thousands more from death. Our success will also have a direct impact on saving young people from illness and suffering, keep families healthy and finally eliminating mother to child transmission.

There is a lot of work to do. We must begin by boldly facing our challenges in over-burdened healthcare facilities, so that nurses and doctors can remain compassionate and provide quality care. Therefore, keeping people free from disease and keeping HIV-positives healthy will go far to alleviate the pressures on health care workers and decongest health facilities. New schedules of clinical visits for stable patients and successful implementation of task shifting will also make adhering to life-long ART much easier for patients.

Through education, we must also prevent men and women from seeking care long after they have started to become sick. Discordant couples will also benefit from our New 'Treat All' Strategy because now no one should put themselves at risk of HIV infection in relationships and the stigma associated with being HIV positive can further dissolve.

We sincerely hope that the portions of the 2016 Integrated HIV Clinical Care Guidelines contained in this small handbook, assists health care providers towards improved healthcare and overall wellbeing.

If we are successful no one should ever become sick from HIV again – but in the event that they do – let us ensure that they are provided with optimum and quality medical care.

Many Thanks,

Ms. Chipo Petlo
Acting Director, DHAPC
Ministry of Health

Acknowledgments and Foreword

The information contained within this handbook is a condensed version of the full 2016 HIV Integrated Clinical Care Guidelines and reflects the latest scientific updates on HIV care from around the world. As we launch the 'Treat All' Strategy, let us appreciate how far we have come in the struggle against HIV in Botswana. When we first started the ART Programme in 2002, no one dreamt that today we would be poised to become one of the few countries in the world to achieve the UNAIDS 90-90-90 targets. No one could have ever imagined that by 2016 Botswana would ben near to virtually eliminating Mother-to-Child transmission and have rolled-out ART services to all hospitals and over 600 clinics – but we did it. Now with the New HIV "Treat All" Strategy, we have the opportunity to finally gain epidemiologic control of HIV after over 16 years of relentless efforts. What better way to pay our respects to the thousands of Batswana who have lost their lives to HIV.

Moving forward our goals are now focused on rapidly expanding access to ART to prevent morbidity and mortality and improving health service delivery through integration.

A few of the highlights contained within this guidelines handbook include:

- The adoption of new testing algorithms to rapidly scale up HIV testing services and expand our diagnostic capacity.
- Providing Universal Access to ART to everyone who is HIV positive – regardless of his or her immune status.
- Recommendation for the use of combination prevention methods that utilize the latest advancement in HIV care, such as PrEP as well as improvement in comprehensive SRH care.
- Improved TB algorithms with wide spread use of GeneXpert technology.
- Recommendations for improved service delivery with streamlined care for clinical and pharmacy visits for stable patients on ART.

Finally, we would like to take this opportunity to thank the many people who contributed their time, clinical experience and wisdom to creating the 2016 Integrated HIV Clinical Care Guidelines.

Thank you very much,

Ms. Dinah Ramaabya
National Coordinator
National ART Programme
Botswana Ministry of Health

CONTENTS

1. HIV Prevention:

Address sexual and reproductive health at every patient visit.

Healthcare providers can prevent the spread of HIV by helping patients to understand that maintaining sexual and reproductive health is essential to ensure longevity, health and wellbeing.

HIV co-infected and HIV discordant couples should carefully consider their sexual and reproductive health, be supported to prevent unintended pregnancies and plan their desired pregnancies. Health care providers should encourage HIV patients to speak openly about their sexual lives and their reproductive plans and intentions.

Educate patients to understand that using a combination of HIV prevention measures is always best to prevent HIV transmission, these include:

- Testing annually for HIV
- Offering safe male circumcision to all sexually active males
- Avoiding STIs and HIV transmission by always using condoms correctly and consistently
- Using Pre-Exposure Prophylaxis (PrEP) when engaging in high risk sexual activity (such as MCP, Transactional Sex, FSW and MSM)

In discordant sexual partnerships educate clients to understand that:

- The HIV positive partner should always maintain complete viral suppression.
- Partners should understand that even with complete viral suppression there is still a small risk of transmission and so consistent and correct condom use are always necessary.
- Treatment for STI's should happen as soon as symptoms (such as pain, dysuria, penile or vaginal discharge) are detected.

Post Exposure Prophylaxis (PEP)

All healthcare providers (or anyone else who are exposed to infectious materials) must always practice universal precautions. If an exposure to infectious material or blood occurs, immediately (ideally within 1-4 hours) administer PEP. (See Annex 1)

HIV Screening & Testing

Botswana has adopted serial HIV testing algorithms as recommended by the WHO. To eliminate the possibility of an HIV negative person being placed on ART, all HIV positive rapid test results will undergo verification at all ART initiation sites before beginning treatment. The revised HIV testing recommendations are outlined in Table 1 below:

Table 1: HIV Testing Algorithms

HIV Testing Algorithm
1. Perform testing with the first rapid HIV test (T1) for HIV screening. 2. **If negative**, recommend annual HIV testing (or appropriate HIV testing intervals based upon risk exposure as per the National HTC guidelines) and refer to the appropriate HIV prevention services (i.e. SMC, consistent and correct condoms use, PrEP, etc.). 3. **If positive**, repeat with a second rapid HIV test (T2). 4. **If the second rapid HIV test is positive,** this is diagnostic for HIV infection and the patient must be immediately referred and tracked to an ART initiation site. **5. If the second rapid HIV test is negative** (i.e. T1 and T2 are discordant) re-test the client as follows:

a) Repeat rapid HIV testing with Test1 and Test2 **in parallel**

- **If both repeat tests are negative,** the patient is diagnosed as HIV negative. Recommend annual HIV testing, etc. (as outline in Step #2 above).
- **If both repeat test are positive,** this is diagnostic for HIV infection and the patients must be immediately referred and tracked to an ART initiation site.
- **If the repeat tests remain discordant (one positive and one negative):**
  - **If in a government facility:** Send a blood specimen for ELISA testing and further investigation at the HIV Reference Laboratory and ask the patient to return in 2 weeks for the result.
  - **If in an approved Routine Testing Center (i.e. NGOs): Use a tie-breaker (T3).** If (after repeat of T1&T2 in parallel) **Test 3 is negative (T1+T2-T3-)** the client is reported as negative for HIV infection. Recommend annual HIV testing, etc. (as outlined in Step #2).
  - **If (after repeat of T1 & T2 in parallel) Test 3 is positive (T1+T2-T3+) consider this result as inconclusive.** Send a blood specimen for ELISA testing and further investigation at the HIV Reference Laboratory and ask the patient to return in 2 weeks for the result.
  - **However, if tie-breaker is not available:** Send a blood specimen for ELISA testing and further investigation at the HIV Reference Laboratory and ask the patient to return in 2 weeks for the result.

HIV Testing Verification

FOR PATIENTS WHO PRESENT FOR ART INITIATION WITH A POSITIVE HIV DIAGNOSIS:
Perform verification of HIV diagnosis as follows:
1. Perform verification using two rapid HIV tests T1 & T2 in parallel.
2. **If both verification tests are negative,** the patient is diagnosed as HIV negative. Recommend annual HIV testing, etc. (as outline in Step #2 above).
3. **If both verification tests are positive,** proceed with ART initiation.
4. **If verification tests are discordant** (one positive and one negative) send blood specimen for ELISA Testing and further investigation at the HIV Reference Laboratory and ask the patient to return in 2 weeks for the result.

Patients < 18 months of age

All HIV exposed babies must complete DNA PCR testing by 6 weeks of age. Dried Blood Spot (DBS) is the preferred specimen collection method.

Immediately refer any infant, who is found to be positive for ART initiation, without waiting for a confirmatory DNA PCR test result.

All children identified as negative by 6 weeks, who do not breastfeed, must undergo rapid HIV testing (as outlined above) at 18 months.

All children identified as negative by 6 weeks, who are breastfed, should have repeat HIV testing 6 weeks after cessation of breastfeeding (if <18 months use DNA PCR-DBS, if ≥ 18months use rapid tests as outlined above).

HIV-exposed babies should be clinically evaluated monthly at the child welfare clinic to detect the development of O.I.s or other HIV related illness.

- **Discuss any HIV-exposed babies with WHO clinical stage 2, 3, or 4 conditions** with a pediatric HIV Specialist for consideration for ART.
- **If DNA test results have not returned within one month** – call the lab and track the results.

To ensure linkage, record mother's and/or relative's cell number and National Identification Number on all requisition sheets.

Testing Adolescents

The attorney General advises that the *Botswana Family Planning General Policy Guidelines and Service Standards* guide the testing of minors. This policy states that: "…teenagers are to be provided with appropriate family planning methods on request after adequate counseling." In other words, if the counselor is satisfied that a young person is mature enough to fully understand his or her behavior and the consequences of that behavior, parental consent is not necessary in order to receive services. **However, it is always best and preferred that parents accompany adolescents for HIV testing and receiving results.**

Pregnant adolescents do not need the consent of their parents to be tested for HIV or to join the PMTCT programme, and parents do not have to be present during counseling. Adolescents may choose to have a parent or another adult with them to provide the necessary support. This option should be discussed with the client and encouraged. It is also important for family members who will be assisting with the baby to be involved.

Special Caution for Pregnant Women found to be HIV Negative:

Pregnant Women who test HIV negative must receive ongoing counseling regarding safe sex practices to avoid undetected HIV infection during late pregnancy. Advise HIV negative mothers that repeat HIV testing should always be completed whenever they have a possible exposure to HIV during pregnancy.

All HIV negative pregnant women must repeat HIV testing every three months, with documented results in the 3rd Trimester/Delivery and 6 weeks post-delivery. If breastfeeding, continue to test for HIV every three months.

Pre Exposure Prophylaxis

(Available now in the private sector and in 2017 within the public sector)

Pre-Exposure Prophylaxis is an HIV prevention strategy that uses ART to protect HIV-negative people at high risk from HIV infection.

PrEP is only recommended for high-risk populations.

Who can be placed on PrEP:

- Individuals who engage in high risk sexual behavior (FSW, MSM, transactional sex)
- HIV negative partner in discordant couples
- Discordant couples attempting to conceive
- Women or men who cannot negotiate safe sex with their partners
- People who engage in multiple current sexual partnerships
- IV Drug Users

Educate Patients that Protection of PrEP Varies between Men and Women

- Studies have shown that PrEP to be more effective in men in African settings.
- Concentrations of TRU in vagina and cervix are lower than those found in the rectum.
- Women may need near perfect adherence to have adequate protection against HIV during vaginal sex.

- Protective levels of TRU are usually reached in the rectum within 1 week and for adequate vaginal concentrations within 3 weeks.

PrEP Clinical Management

Prescribe: TRU 1 tablet PO QD

It is the healthcare provider's responsibility to have the clinical capacity and mechanisms in place to adequately monitor all patients who are placed on PrEP, as follows:

- Maintain close clinical and laboratory monitoring (q 3 months)
- Complete renal function monitoring is required as for all TRU containing regimens (CrCl)
- Complete HIV testing every 3 months
- Recommend that correct and consistent condoms must always be used
- Screen for STIs at every clinical visit
- Provide adequate counseling so that patients understand the risks associated with poor adherence.

2. Sexual Reproductive Health

HIV-infected women and their partners have a fundamental human right to 'a satisfying and safe sexual and reproductive life.' HIV-infected women and couples must be supported to effectively prevent unintended pregnancies, and to have planned, safe pregnancies when they desire. Preventing unintended pregnancies leads to improvements in maternal and child health and prevents mother to child transmission of HIV.

Healthcare providers should encourage HIV-infected patients to speak openly about their reproductive plans and desires and assist them to make well-informed decisions regarding pregnancy prevention or pregnancy planning. ***Good clinical care in this regard means identifying the right contraceptive method in terms of safety, effectiveness, and acceptability for the right women at the right time. HIV-affected women and couples should be asked regularly in a non-judgmental way about their desires/plans for future childbearing and if they chose be offered comprehensive counseling regarding appropriate contraception.***

Inform patients about the range of contraceptive methods available:

- Male and female condoms, the intrauterine device (IUD, aka "loop" or "coil"), the subdermal contraceptive implant, the injectable contraceptive, combined and progestin-only oral contraceptive pills, the contraceptive ring, the contraceptive patch, and female and male sterilization)
- Decision-making about the most appropriate contraceptive should be informed by the World Health Organization Medical Eligibility Criteria (MEC) guidance and patient preference (see Annex 2).
- Always recommend "dual method" use for the most effective prevention of both HIV transmission and pregnancy (i.e. the use of a male or female condom along with another effective method of contraception).

(Refer to the 2016 HIV Integrated Care Guidelines for comprehensive information regarding all contraceptive methods available. For a summary of contraception methods available see Annex 1A)

Discordant Couples who wish to have children:

- Provide adequate counseling on the risks of unprotected sex, health optimization prior to pregnancy, safer conception options, use of PrEP in the private sector, and options for adoption and fostering.

- Options for safer conception include timed conception (i.e. confine unprotected intercourse to the time of peak fertility in the woman's menstrual cycle), self-insemination and assisted reproduction.

Pregnant women who test HIV negative at their first ANC clinic visit must receive ongoing counseling regarding safe sex, to avoid undetected HIV infection during pregnancy and MTCT.

3. PMTCT

HIV Positive Women on ART Considering Pregnancy:
In order to minimize the risk of a negative pregnancy outcome, recommend that the following conditions are met prior to becoming pregnant:

- Viral load suppression to: <400 copies/mL
- CD_4 count above 200 cell/µL
- Stable on ART for no less than 2 years

Advise women with detectable viral loads to postpone pregnancy until they have been successfully placed on a fully suppressive regimen. Contact an HIV specialist as needed.

Place All HIV Positive ART Naïve Pregnant Women on ART as soon as possible. Always Prioritize HIV Positive Pregnant Women for Initiation

- During Labour: All HIV positive women – regardless of their ART regimens - should receive supplemental AZT 300 mg every three hours not to exceed 1,500 mg.

ART Recommendations for ALL Treatment Naïve Pregnant Women

The principles of ART in HIV-infected pregnant women, including dosages, laboratory monitoring, and criteria for treatment success or failure, are unchanged from other adults. **Initiate ART – even late in pregnancy - unless in advanced second stage of labour,** ***there is no stage of pregnancy that is too early or too late to begin ART.***

Initiate: TRU 1 Tablet PO OD + DTG 50mg PO OD
If renal insufficiency without CVD risk use: ***ABC/3TC/DTG*** *If renal insufficiency with CVD risk: Discuss with HIV Specialist*
For diabetics taking metformin, reduce dose with assistance from HIV Specialist, maximum dosage of Metformin is not to exceed 1,000 mg daily

HIV Positive Women STABLE on ART Who Become Pregnant:
Women who are clinically stable with viral loads <400 copies/ µL **should remain on their current ART regimen throughout pregnancy and delivery.**

HIV Positive Women Already on ART but NOT STABLE Who Become Pregnant:
- Clinically evaluate all pregnant women who are not clinically stable or not virally suppressed, to determine and correct the causes of non-suppression or illness, as a matter of urgency.
- Contact an HIV Specialist as needed to ensure complete virologic suppression before delivery.

Assessment for ART in pregnancy is based upon timing of presentation:

Give HIV positive women priority to begin ART at all health facilities. Ensure that women have adequate social support and understand the importance of strict adherence. However, do not delay initiation; complicated social circumstances that could negatively impact adherence should be discussed with senior HIV clinicians or HIV specialists.

< 28 Weeks Gestation:

Begin ART within 1-2 weeks of presentation at health facility. Process all baseline labs as a priority.

- If labs are normal immediately initiate: **TRU 1 tablet PO OD + DTG 50mg PO OD**
- If labs are out of range, determine cause and take corrective measures as matter of urgency. Contact HIV specialists as needed.

> 28 Weeks gestation:

Place all late presenting HIV positive pregnant women on ART as soon as possible.

If clinically stable initiate TRU/DTG (as above) immediately, without waiting for laboratory results

- Process all baseline labs as priority labs.
- Once lab results return, if necessary modify regimen appropriately.
    - *If CrCl is less than 60 cc/min switch to ABC/3TC/DTG and dose reduce if required*
    - *If CVD risk is also present, discuss with HIV Specialist*
- Ask women to return to the clinic with an adherence partner within 5 working days of initiation to receive adherence counseling to ensure long-term adherence.
- Unless viral suppression can be documented <400 copies/mL, late presenters **SHOULD BE ADVISED NOT TO BREASTFEED**

For Women Identified HIV Positive at Labour

- **Begin TRU/DTG immediately**
- Give supplemental AZT 300mg every 3 hours, not to exceed 1500 mg
- At the earliest convenience complete appropriate adherence counseling for life-long ART while admitted.
- **ENSURE THAT THERE IS LINKAGE TO ART CARE UPON DISCHARGE**
- **WOMEN NEWLY DIAGNOSED WITH HIV WHO PRESENT AT LABOUR BE ADVISED NOT TO BREASTFEED.**

Other Special Considerations for HIV Positive Pregnant Women

- Ensure that all HIV+ women placed on ART during labour have been linked to an appropriate ART facility for long-term HIV care after delivery.
- Provide HIV adherence counseling for mothers and their partners as required.
- Evaluate and aggressively treat all sexually transmitted infection, including syphilis.
- Treat any episode of genital HSV with acyclovir.
    - **Dosage**: Acyclovir 800 mg PO TDS until lesions are contained.
- If necessary, obtain Specialist approval for use of acyclovir for this indication.
- At every visit counsel mothers on the importance of using condoms consistently and correctly throughout pregnancy.
- **Ensure that all causes of Anemia are identified and corrected**
    - If recently initiated on CBV and virally suppressed, switch from AZT containing regimens to TRU/DTG or ABC/3TC/DTG (depending on clinical condition and treatment history)
    - If unsuppressed, discuss modified regimen options with a HIV specialist.

Obstetric measures to reduce MTCT

- Avoid early artificial rupture of membranes
- Avoid routine episiotomies

- Use non-traumatizing suction cups on vacuum extractors, when assisted vaginal delivery is indicated
- Avoid fetal scalp puncture
- Ensure that delivery occurs within 4 hours after rupture of membranes

Neonatal ARV Interventions for PMTCT

Administer a short-course of AZT to the infant (regardless of whether or not the mother received any ARVs during pregnancy or delivery) as soon as possible after delivery at least within 72 hours, in order to maximize PMTCT as follows:

- Begin AZT 4mg/kg PO every 12 hours for 4 weeks.
- Preterm or low birth weight, give AZT dose is 2mg/kg PO every 12 hours for the first 2 weeks, then increase to 2mg/kg PO every 8 hours (TDS) for the final 2 weeks.
- **HIV-exposed infants brought in > 72 hours after birth should not receive AZT prophylaxis** but rather should be referred to an HIV specialist or ARV clinic.
- **In cases where mothers present late for ART initiation and are unlikely to be virally suppressed*:***
    - ***Begin full ART for infants AZT/3TC/NVP (as outlined in Table 2 below).***
    - ***At 1 month test high- risk infants to determine their HIV status in order to decide whether to continue ART.***
    - ***For infants testing positive, switch to ABC/3TC/ALU (as outlined in Table 2 below)***
- **Diligently monitor and report all adverse birth outcomes of HIV positive women regardless of their ART regimens.**

Infant Feeding

Breast is Best – Only when it is Safe!

HIV positive women who are suppressed on ART should be encouraged to breastfeed their children for a maximum of 6 months. However, there are circumstances when HIV positive mothers are not able to breastfeed because of their medical condition or because their HIV is not fully suppressed (<400 copies/mL). Likewise, there are situations when formula feeding is not safe for example, due to unclean water supply. Therefore, before recommending (or not recommending) breastfeeding to HIV positive women consider all aspects of a mother's social and medical situation and determine whether formula feeding is AFASS compliant (Affordable, Feasible, Acceptable, Sustainable and Safe).

The risk of HIV transmission from breastfeeding outside of research conditions in Botswana is unknown. It therefore remains the right of every HIV positive mother to decide whether or not to breastfeed her child and her decisions should be respected.

Breastfeeding HIV negative mothers should complete HIV testing every 3 months

Infant formula will remain available within the public sector to any HIV-infected women who chooses not to breastfeed.

Infant feeding counseling should be provided to ALL pregnant women starting from ANC.

- **Advise the following HIV positive pregnant women NOT to breastfeed:**
  - **Not on ART**
  - **On ART without documented viral suppression <400 copies/mL within the last three months.**
  - **Diagnosed HIV positive at time of labour.**
- If breastfeeding is chosen, advise women to exclusively breastfeed for the first 6 months of life, transition to formula feeding at 6 months, if AFASS conditions are met.
- Introduce complimentary feeding as 6 months, refer to the 2016 HIV Integrated Clinical Care Guidelines for safe instructions on weaning.
- If formula feeding is AFASS, exclusively formula feed for the first 6 months of life.
- Introduce complimentary foods at 6 months and continue formula feeding until 12 months of age.

4. Initiation of ART in Children & Adolescents

Ensure that children's complete ART history is well documented. Include history of opportunistic infections, co-morbidities and PMTCT regimens. Always address the following points prior to initiation of ART in all pediatric and adolescent patients:

- Who will be primarily responsible for giving the child medications and supervising adherence?
- If there are multiple caregivers, how will coordination between these caregivers be achieved?
- Who will ensure medication adherence if the usual caregiver(s) is absent?
- What is the caregivers' knowledge of the ART?
- What age-appropriate role will the child play in ART adherence?
- What is the child's understanding of the medications and his/her HIV status?
- If the child is able to appropriately dose medications, what adult will be responsible for supervising the child?

Cotrimaxazole For Infants and Children

- Give CTX to all HIV-exposed infants until DBS results are returned and while breastfeeding. Continue until 6 weeks after breastfeeding cessation until HIV testing results are documented.
- HIV positive children 1 to 5 years: CTX if CD4% <25%
- HIV positive children >5 years: CTX if CD4% <15% or absolute CD4 count is <200 cells / µL.
- Other pediatric indications for CTX include: Active WHO stage 2, 3, or 4 conditions, virological failure (unless suppressed) or HIV positive children who have not yet initiated on ART for any reason.

Initiate ART in Pediatric Patients as outlined in Table 2 below:

Table 2: ART Regimens for New and Previously Initiated Children and Infants

PEDIATRICS	Age Weight	1st Line	1st Line Modifications for toxicities	2nd Line
Initiations Beginning 2016	<1 month	AZT/3TC/NVP* ***(switch infants to ABC/3TC/ALU at 1 month)***	**ABC or NVP Rash:** CBV/ALU	**Based on R Testing Results & Consultation with HIV Specialist**
	>1 month to 3 years	ABC/3TC/ALU		
	>3 yrs <40Kg	ABC/3TC/EFV	**ABC Rash:** CBV/EFV **CNS Toxicity:** ABC/3TC/ALU	

All Pediatric Patients Failing 1st Line regardless of their regimen will be Resistance Tested to determine 2nd line with assistance of HIV specialist
****Except infants whose mothers received sdNVP – then 1st Line ABC/FTC/ALU***

PEDIATRICS	Age Weight	1st Line	1st Line Modifications for toxicities	2nd Line	2nd Line Modifications
Initiations Prior to 2016	>3 yrs <40kg	CBV/EFV CBV/NVP	**AZT Anemia:** ABC/3TC/EFV or NVP **EFV CNS:** CBV/ALU	CBV/ALU ABC/3TC/ALU	**AZT Anemia and/or** Discuss with Pediatric Specialist **ALU Toxicity:** CBV + RAL ABC/3TC/RAL
		ABC/3TC/NVP ABC/3TC/EFV	**ABC Rash:** CBV/3TC/EFV or NVP EFV CNS: **EFV CNS:** CBV/ALU	CBV/ATZ/r TRU/ATZ/r	**AZT Anemia and/or** **TDF Renal Toxicity:** ABC/3TC/ATZ/r

All 2nd Line Failures regardless of their regimens will be Resistance Tested to determine 3rd line with assistance of HIV Specialist

Table 3: WHO Simplified CTX Dosing for Pediatric Patients

Age & Weight	Recommended Daily Dose	Suspension (5MLsyrup= 200mg/40mg	Child Tablet	Single Strength adult tablet 400mg/80mg	Double Strength adult tablet 800mg/160mg
6wks – 6 months <5 kg	100 mg sulfamethoxzole 20mg trimethoprim	2.5mL	1 tablet	¼ tablet	-
6mons – 5 years 5-15 kg	200 mg sulfamethoxzole 40mg trimethoprim	5 mL	2 tablets	Half tablet	-
6 years to 14 years	400 mg sulfamethoxzole 80 mg trimethoprim	10 mL	4 tablets	1 tablet	Half tablet
Post pubertal adolescents and adults	800 mg sulfamethoxzole 160mg trimethoprim	-	-	2 tablets	1 tablet

Pediatric ART Initiation Considerations and Key Points

Fixed dose combinations should be used as much as possible to improve adherence

- For infants whose mothers received sdNVP under previous guidelines as a late presenter for PMTCT:
  Less than 1 month of age: Discuss regimens with pediatric specialist
  > 1 month < 3 years of age, 1st Line: CBV + LPV/r
  > 3 years of age, 1st Line: CBV + EFV > 3 year
- **Chest X-rays** at baseline are only indicated when symptoms are suggestive of pulmonary disease, if reading is delayed discuss with HIV specialist to avoid unnecessary delays of ART initiation.
- Whenever CD4 counts are above 250 cells m/L in women or above 400 cells m/L in men, do not initiate **NVP containing regimens.**
- No patient adult or pediatric should be treated with D4T or Saquinavir containing regimens. Discuss with specialist as required.

5. ART Initiation in Adults and Adolescents

Ensure that patient's complete ART history is well documented.
Include the date of HIV diagnosis, history of opportunistic infections, co-morbidities and PMTCT regimens.

Adolescent Special Considerations

All clinics should identify staff with interest in adolescent care, which can provide continuity of care with HIV-infected adolescents. These designated staff members can form a 'therapeutic alliance' with adolescents, to help them handle challenges to their wellbeing. These 'continuity-of-care' providers should explore with the adolescent issues of sexuality, safe sex, substance abuse, barriers to adherence, and community support. Notwithstanding the importance of family support for the

adolescent, 'parental consent is not necessary to receive services' including HIV testing and SRH services.

Initiate ART in Adults & Adolescents (>40kg) as outlined in Table 4 below:

Table 4: ART Regimens for New and Previously Initiated Adults and Adolescents

ALL ADULTS & ADOLESCENTS (>40kg)	1st Line	1st Line Modifications	2nd Line
Initiations Beginning 2016 ***(Including pregnant women)***	Truvada + Dolutegravir	**TDF renal toxicity w/o CVD risk:** ABC/3TC/DTG **TDF renal toxicity or insufficiency with CVD risk or DTG Toxicity:** Discuss w specialist	**Based on Resistance Testing Results & Consultation with HIV Specialist**
All Adults Failing 1st Line with DTG containing regimens will be resistance tested to determine 2nd line with assistance from an HIV specialist.			

ALL ADULTS & ADOLESCENTS (>40kg)	1st Line	1st Line Modifications	2nd Line	2nd Line Modifications
Initiations Prior to 2016	TDF/FTC/EFV TRU/NVP CBV/EFV CBV/NVP ABC/3TC/NVP ABC/3TC/EFV	**TDF renal toxicity w/o CVD risk:** ABC/3TC/DTG *(If CVD rash: Consult HIV specialist)* **CNS Toxicity and/or Hepatic Toxicity:** TRU/DTG	CBV/ALU TRU/ALU CBV/ATA/r TRU/ATA/r	**AZT Anemia** and/or **TDF Renal Toxicity:** ABC/3TC/DTG
All adult 2nd Line failures (regardless of their regimens) will be resistance tested to determine 3rd line with assistance from an HIV specialist.				

Notes:

- Document complete treatment histories into all patient charts, noting dates of toxicities, defaults, treatment failures.
- Diabetics on Metformin must have dosage reduced (maximum daily dose 1,000mg) discuss with HIV specialist
- Creatinine Clearance Calculation: **MALES**: $\frac{(140\text{-age}) \times \text{Body Wt in Kg}}{\text{Serum Creatinine} \times 72}$ **FEMALES**: Male formula x 0.85

Although the majority of new patients will be initiated on DTG containing regimens, in the event that a patient requires a modification to first line remember the following:

- Avoid initiation with NNRTIs for any woman who received sdNVP under previous guidelines.
- When CD4 is >250 cells/μL in women or >400 cells in men, do not switch to NVP containing regimens.

Special Consideration for Patients with Advanced HIV:

For patients who present for ART initiation with Advanced HIV disease: CD4 ≤100 cell/mL or WHO Stage 3 & 4 disease, at baseline clinical visit include the following:

- Cryptococcal Antigen test (CRAG)
- Referral for screening of CMV retinitis at nearest ophthalmology center

Adult and Adolescent (>40kg) ART Regimens

Until officially notified otherwise, keep all stable patients (those who are virally suppressed without toxicities or history of poor adherence) on their current ART regimens. Beginning in 2017, older ART regimens will begin to be phased out. The Ministry of Health will communicate information regarding prioritization for switching treatment groups and all treatment options at a later date.

However, patients on older ART regimens who develop toxicities should be switched to DTG containing regimens, whenever possible. NRTI backbones for these treatment switches must be made based upon previous treatment histories and the presence of full virological suppression. Seek advice from HIV Specialists as required.

Revised Guidance for Adherence counseling with "Treat All"

The adoption of "Treat All" could see increases in the numbers of patients who default treatment or exercise poor adherence unless health care providers who initiate ART clearly educate patients on the importance of both early treatment and strict adherence. Patients should be made to understand the following:

- Early initiation of ART may decrease mortality and morbidity by more than 60%
- Early initiation of ART will decrease the chances of contracting TB and developing cancer.
- Early initiation of ART will protect their sexual partners from HIV transmission
- Although they may be healthy now – initiating ART is currently the only way known to prevent the eventual decline of immune function and development of opportunistic infections.
- Early initiation of ART is the best way to ensure normal life expectancy.

Recommendations for "Treat All" Adherence Counseling:

Educate and discuss the following topics with all patients before initiating ART:

1. For now, there is no cure for HIV.
2. Without taking the HIV prevention precautions, HIV-infected people can easily pass HIV to their sexual partners.
3. Taking ART is a life-long commitment
4. Although they may not be sick now, it is just a matter of time before HIV will destroy their immune system and cause opportunistic infections and/or cancers.
5. Defaulting from treatment will decrease their chances for remaining disease free despite HIV infection and enjoying a normal life expectancy.
6. Whenever their life circumstances change and they want to stop ART, they should first seek the advice of their healthcare providers.
7. People who start ART when they are healthy with higher CD4 counts, experience less side effects to ART.

8. HIV-infection is a chronic disease that must be managed like any other chronic disease, with regular medical consultations and adherence to medications.
9. Patients should seek mental health support when their circumstances cause depression, self-stigma and/or the desire to stop taking ART.
10. Life-long ART is only guarantee there is for HIV-infected people to live normal, happy and healthy and lives.

Ensure that all Patient Information (including cell phone numbers) is current for purposes of tracking patients as necessary.

Depression

Properly address depression in patients identified with psych-social challenges, particularly those who are failing ART. Provide on-going counseling services and prescribe antidepressant medication when necessary.

Cardiovascular Disease, ART & HIV

All classes of ART can cause elevated total cholesterol (TC) and triglycerides (TG), which may lead to serious long term, cardiovascular and/or cerebrovascular disease. Cardiovascular related morbidities, regardless of whether they are related to ART or not, must be addressed promptly including modification of vascular risk factors such as prior stroke, heart attack, peripheral arterial disease, smoking, hypertension, diabetes, BMI >25 and elevated waist-hip ratio (Males >94cm, Females >80cm).

Elevated lipids can appear within the first months of initiating ART

- The most significant lipid abnormalities occur with d4T, AZT and PIs, including LPV/r.
- NNRTIs may cause relatively minor increases in cholesterol (EFV > NVP).
- Atazanavir and integrase inhibitors (RAL & DTG) are most lipid friendly
- Elevated TG may cause pancreatitis

Before initiating PI based ART

- Determine the baseline non-fasting lipid profile: TC, LDL-C, HDL-C and TG.
- Inquire about any family history of heart related disease, diabetes mellitus II.
- **Screen all patients on PI-based ART annually**

Clinically significant LDL thresholds/goals vary according to the presence of known vascular risk factors or disease according to the following CVD risk groups:

Table 5: Recommendations for LDL Levels in CVD Risk Groups 1-3

CVD Risk Groups	Clinical History	Treatment	Notes
Group 1	• Prior Stroke • Heart Attack • Peripheral heart disease • DM Type 2	Atorvastatin 80mg QD (or Rosuvastatin 20mg QD) Aspirin 75-150 mg	**If taking Ritonavir** Adjust: Atorvastatin 10mg Rosuvastatin 10mg **Discuss ABC use w HIV Specialist**
Follow up LDL results from Baseline lipid profile for Group 1 should be <2.5 mmol/L			

Group 2	**Three or more of the following cardio risk factors:** Smoking, HTN, BMI>25, Waist circumference (Males >94cm, Females >80cm), >55 years of age (females), >65 years of age (males), LDL>5.1 mmol/L	Atorvastatin 40mg QD or Rosuvastatin 10mg QD	**Discuss ABC use w HIV Specialist**
Follow up LDL results from Baseline lipid profile for Group 2 should be <3.3 mmol/L			
Group 3	· No CVD Factors	None	If TC >5mmol/L, advise life-style changes & repeat lipid profile in 4-8 weeks
Follow up LDL results from Baseline lipid profile for Group 3 should be <5.1 mmol/L			

As a rule, TC should be < 4.5 mmol/L. Any increased LDL (as above) and/or TC > 5.0 mmol/L requires the following stepwise approach:

- Switch LPV/r regimens to Atazanavir or Raltegravir or Dolutegravir with the approval of an HIV Specialist.
- Discuss the use of Abacavir with HIV specialist in all group 1 to 3 CVD risk patients.
- Educate patients on the risks of elevated lipids.
- Initiate dietary interventions including nutritionist referral for counseling, if available.
- Recommend regular exercise, as indicated by the patient's overall health and cardiovascular status.
- Aggressively manage all other associated vascular risk factors: cigarette smoking, hypertension, obesity, diabetes, pre-diabetes (HBA1C 5.8-6.3%), and stress *(see The Botswana Primary Care Guidelines).*

If the above interventions are not successful, prescribe the following medications for group 2 & 3 patients:

- **For Group 2**: Atorvastatin 10-20 mg PO QD (or Rosuvastatin 10-20mg QD) (titrate as necessary).
- **For Group 3**: Atorvastatin 5-10mg QD (or Rosuvastatin 5mg QD) (titrate as necessary)
- **Monitor for new muscle pain & rhabdomyolysis (with CPK) for all patients**
- For increased Triglycerides (once DM and other causes such as alcohol abuse are excluded) prescribe: bezafibrate 200mg TDS or BD
- Consider Aspirin 75-150mg QD for all group 2 patients if >50 years old
- **Follow-up lipids every 3 months until normal, and thereafter annually**
- **Consultation with an HIV Specialist if the above interventions are unsuccessful.**

Co-Infection with Hepatitis

- All patients found to be Hepatitis Surface Antigen (HBsAg) positive should be initiated on Truvada (Tenofovir + FTC) containing regimens as these drugs are also active against HBV.
- If TRU cannot be used discuss with an HIV specialist.
- Ensure that patient's medical records reflect HBsAg positivity so that immune reconstitution is properly identified and addressed.
- IF TRU must be stopped for any reason or if treatment modification is required, discuss with an HIV specialist to avoid reactivation of HBV and hepatocellular damage.
- Co-infected patients should be educated to not stop TRU without discussing this with their health care providers.
- Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage

ART Treatment Failure

Monitor viral load results closely to detect virologic failure to preserve future treatment options and prevent the development of O.I.s

- All clinics must develop and implement effective and sustainable procedures for reviewing laboratory reports with 48 hours of receiving results, paying particular attention to abnormal and detectable viral loads results.
- All clinics must establish an ongoing failure management clinic and failure management team to address treatment failure in a comprehensive manner, including adequate psychosocial and mental health support.

Definition of Treatment Failure:

- Viral load does not suppress to <400 copies/mL by 6 months after ART initiation.
- After documented virologic suppression to <400 copies/mL, the viral loads becomes detectable again and is confirmed by two priority viral loads.
- Immunologic failure (CD4<200 after more than 1 year on ART) with full viral suppression **does not warrant a regimen change.** Discuss with an HIV specialist as required.

Addressing Treatment Failure

Remember: If non-resistance causes of treatment failure are not promptly addressed, and if ongoing viremia persists in the presence of ART, HIV resistance will eventually develop.

Address ART Treatment Failure with a step-wise approach:

1. **Identify causes of failure**:
   - Non-adherence, incorrect dosage of ART, adverse side effects, drug-drug interactions, GI disturbance and malabsorption.
   - Consider common adverse drug-drug reactions such as: Rifampicin and PIs, carbamazepine and EFV, antacids, use of traditional medicines.
2. **Identify and address all non-resistance causes of failure:**
   - Intensify adherence interventions, correct dosages, treat gastroenteritis, and address any drug-drug interactions.
3. **Repeat priority viral load measurements in 4-6 weeks**
   - If suppressed repeat PVL again in 3 months, if still suppressed, return to q 6 month VL monitoring intervals.
   - **If not suppressed,** repeat PVL again at 4-6 weeks to ensure VL is fully suppressed or trending down by at least one log.
   - **If VL is not trending down by at least one log assume resistance has developed and change the entire regimen**. **Do not continue to send repeated PVLs indefinitely.**
   - Continue PVL monitoring every 4-6 weeks if VL continues to decrease until full virologic suppression is achieved to <400 copies/ µL.
   - **By six months all VL that are trending down should be fully suppressed, if not** discuss cases with an HIV specialist.
4. **In pediatric cases, full suppression may take longer than 6 weeks**.
   - Once non-resistant causes of treatment failure are addressed, continue to monitor children monthly, until full suppression is achieved but not longer than six months. Consult HIV specialists as needed.

Indications for Resistance Testing

- All pediatric first line failures
- All adult first line failures using DTG
- All adult second line failures
- Patients with complicated treatment histories and highly treatment experienced

Indications for Priority Viral Loads and other Laboratories

- All viral loads on patients under 20 years of age
- Repeat viral loads to confirm virologic failure
- Viral loads done before switching or substituting 1 or more medication (if not completed within the last three months)
- Viral loads done before full treatment switch
- Follow up 4-6 week viral load after treatment switch
- Follow up viral loads after adjustments made for poor adherence, drug-drug interactions, adverse side effects or severe GI disturbance.
- Viral loads on all pregnant women

Remember: Always Clearly Label PRIORITY on Lab Requisition Forms

Scenarios highly suggestive of treatment failure – when lab results are not available:

- Development of an opportunistic infection (WHO stage 3 or 4)
- Any drop of CD_4 count less than baseline value, or a 50% decline in CD_4 cell count from the highest value while on treatment.
- Simultaneous clinical and immunologic deterioration.

Indications for consultation with HIV Specialist include:

- Failure to achieve full suppression <400 cell/ µL in a pediatric patient after 6 months on ART.
- Infants whose DNA-PCR results are pending, and who have clinical stage 2, 3, or 4 conditions.
- ART initiation of infants <1 month of age.
- Evaluations of treatment failure in the absence of resistance testing results.
- Immunologic and/or clinical failure with full virologic suppression as required.
- Ordering and interpretation of genotypic resistance testing
- Designing 2nd and 3rd line regimens after completion of resistance testing.
- Difficult decisions regarding PEP or PrEP
- Any failures with DTG.
- Approvals for special orders for: Darunavir, Raltegravir, Atazanavir/r, and Ritonavir

6. TB /HIV Co-Infection

Clinical evidence shows that early ART initiation reduces the risk of death in TB/HIV patients. This is particularly important at low CD_4 counts. ART naïve patients (or those restarting treatment for any reason) with low CD_4 counts should start ART as soon as they are tolerating ATT and at latest by 2 weeks of the initial phase of ATT. Close monitoring for signs or symptoms of hepatitis and worsening of TB due to IRIS is essential. All TB/HIV co-infected patients must receive prompt referral and timely follow-up in HIV care facilities, including counseling, social support and home-based care as necessary.

People living with HIV must be routinely screened for TB in all places where they receive medical care including: ARV clinics, hospital wards, PMTCT facilities & HIV Testing and Counseling Centers.

TB Screening results must be documented at each and every patient encounter.

Intensified Case Finding (ICF)

ICF includes screening for signs and symptoms of TB by asking patients whether they have cough, fever, night sweats, weight loss and evidence of lymphadenopathy. No one symptom is diagnostic for TB. Therefore ***cough of any duration***, fever, night sweats, weight loss or presence of enlarged lymph nodes in an HIV patient should prompt an evaluation.

> **Always complete a comprehensive physical examination of HIV patients during routine follow up visits in order to rule out TB.**

TB screening in children must also include asking about decreased playfulness and failure to gain weight (as evidenced on the under 5 card). Most young children acquire TB from an adult with smear positive TB. Therefore, it is essential to ask about TB exposure in the household as part of the symptom screen.

> ***Remember**: A detectable viral load in a previously suppressed patient may be the first sign of TB disease. While assessing other causes of ARV treatment failure such as adherence, all failing patients must be carefully screened for TB.*

TB Screening Signs and Symptoms:

- Cough, fever, night sweats, weight loss, and ***lymphadenopathy of any duration***
- Detectable viral load must also be closely evaluated for TB co-infection.
- **In children also include:** Decreased playfulness, failure to gain weight, and TB exposure in the household.
- ***Remember:** Asymptomatic children with TB contact are candidates for IPT (refer to IPT Section.*

A positive response or finding to any one of these signs and symptoms requires further evaluation for TB as outlines in Annex 4

Indications for Culture and DST:

All High Risk Drug Resistant TB Groups

- Symptomatic individuals at higher risk of MDR-TB such as Lab workers, MDR-TB/XDR TB contacts, Health Care Workers including cleaners and drivers
- All retreatment patients regardless of reason (failure, relapse, or default)
- Patient with previous history of TB treatment including those who received ATT for >1 month
- People living in congregate settings: Prisoners, Prison wardens, refugees
- Ex-miners

Groups with low TB smear sensitivity

- All patients with HIV but in particular, children and those with advanced immunosuppression (i.e., CD_4 <100 cells/ µL).
- Patients with suspected cryptogenic TB should have blood taken for TB culture and sent to the NTRL. The blood specimen should be collected in special media culture bottles available from the National Health Laboratory.

Isoniazid Preventive Therapy (IPT) for Children

It is important to note that any child, regardless of age, who is asymptomatic but has been identified as an MDR-TB contact should not receive IPT.

- All children < 5 years of age, who are in contact with TB patients should be fully assessed for HIV and TB. Regardless of their HIV status, those children who are not clinically symptomatic for TB should receive IPT for 6 months.
- All HIV-infected children > 5 years and < 12 years, who are in contact with a TB patient should be fully assessed for TB infection. Those HIV-infected children who are asymptomatic for TB should receive IPT for 6 months.

ART and ATT Co-Administration

For adults & adolescents already on ART who develop TB, follow Table 6 below:

Table 6: ART & ATT Regimens

ART Regimen	Adjustment for ATT
TRU/DTG CBV/DTG ABC/3TC/DTG	**Double dose of DTG to 50mg PO BD** **NOTE:** *Upon completion of ATT ensure that the DTG dose is adjusted back to* ***50mg daily.***
CBV/EFV or NVP TRU/EFV or NVP ABC/EFV or NVP	**Make NO adjustment**
CBV/ATA/r TRU/ATA/r ABC/3TC/ATA/r CBV/LPV/r TRU/LPV/r ABC/3TC/LPV/r	1. Stop ATA/r or LPV/r. 2. Maintain original NRTI backbone 3. Initiate DTG 50mg PO BD 4. Upon completion of ATT make sure that the DTG dose is adjusted back to **50mg daily.**
Highly treatment experienced patients on RAL/DAR and NRTI backbone regimens	Discuss with HIV/TB Specialist
Discuss patients who cannot tolerate DTG regimens with an HIV /TB Specialist	

For ART Naïve Patients Who Develop TB

All HIV patients should promptly begin ART.

Always initiate ATT first, followed by ART as soon as possible but **no later than 8 weeks.**

- Patients with CD4 count <100 cells/µl: start ART as soon as the patient is tolerating ATT
- Patients with CD4 count >100 cells/µl: start ART within 8 weeks.

Patients with Suspected Neurological Involvement or Deranged ALTs

TB/HIV co-infected patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm^3) should receive ART within the first two weeks of initiating ATT. However, exercise caution with severely immunosuppressed patients with suspected neurological involvement or deranged LFTs. Great care must be taken to monitor these patients for hepatitis and worsening of TB due to IRIS (seek advice from TB/HIV specialist if necessary).

ART Regimens in Treatment Naïve TB/HIV Co-infected Patients

Initiate ART in naïve patients as indicated in Table 8.2 below:

Table 7: HIV Treatment Regimens for Adult TB/HIV patients while taking ATT

Line of Therapy	Drug Regimen
First-line: ▪ Adult ▪ Pregnant women a ▪ Adolescent (>40kg)	**TRU 1 tablet PO QD + DTG 50mg PO BD**
Alternative First-line:	TDF/FTC/EFV (Atripla)

Contact TB/HIV specialist in cases for unusual cases or medication stock-outs

Discuss all complicated TB/HIV co-infected patients with HIV & TB Specialist and refer to the 2016 HIV Integrated Clinical Care Guidelines or BNTP Guidelines for further information on treatment management.

Remember: All patients of all ages with active TB must be started on CTX prophylaxis, give OD. If at the end of ATT the CD4 count threshold for continued CTX prophylaxis is not met, CTX should be stopped.

All healthcare workers, especially those who are HIV-infected, must exercise great caution when caring for patients with TB and suspected TB, especially MDR-and XDR. Respiratory isolation precautions must be observed at all times.

7. Treatment for Cryptococcal Meningitis

Data from Botswana shows that 5% of patients with CD4 counts below 100 cells/µL (and 21% of hospital inpatients with CD4 counts below 100 cells/µL) have detectable cryptococcal antigen (CrAg) in their blood. Many of these patients have no symptoms or signs of cryptococcal meningitis, but are at very high risk of developing it.

Screen all patients with CD4 counts below 100 cells/mcL with serum or plasma cryptococcal antigen tests and treat them according to the guidelines below.

Clinical Manifestations:

Disease onset is often subtle, with classic meningeal signs absent in up to 50% of cases. Symptoms usually develop slowly over several weeks, but can occur over days. Neck stiffness is an unreliable sign. Maintain a high degree of suspicion in patients with low CD4 counts (<100 cells/ µL or CD4% <15%) or who report any of the following:

- Headache (often initially of low-grade severity)
- Altered mental status
- Visual disturbances
- Unexplained fever

Complete a comprehensive physical exam (including a full neurological exam) and lumbar puncture in all HIV-infected patients with CD4<200 cell/µL suspected to have cryptococcal meningitis.

A lumbar puncture should be considered an emergent, "opt-out", life-saving procedure that does not require explicit consent. Reassure reluctant patients and their families that the potential benefits of completing an LP far outweigh any risk of complications.

- If a CT of the head can be performed and reviewed within a few hours, it is reasonable to defer a lumbar puncture pending the CT head results for a patient who presents with hemiparesis and other focal neurologic signs. However, **in all other situations, CT is not a requirement for a lumbar puncture**. :
- Complete the following on CSF
  - ***India ink smear and cryptococcal culture***
  - If India ink smear is negative then complete a CSF CRAG
  - Cell count, differential, MCS, and where available, protein and glucose.

In cases displaying lymphocytic meningitis and negative India ink, CRAG and culture, the most likely diagnosis is TB meningitis. Perform a GeneXpert on CSF and TB culture. Begin treatment for TB meningitis and discuss with an HIV/TB specialist.

Treatment: Antifungal Therapy for Adults

Treat Adults and Children for Cryptococcal Meningitis as follows:

Table 8: Antifungal Treatment for Cryptococcal Meningitis

Follow These Steps:	Adults	Paediatrics
1. Induction 2 weeks	*Amphotericin B: 1 mg/kg + Fluconazole 1200 mg daily	Amphotericin B: 1 mg/kg + Fluconazole: 6 mg/kg daily
2. Consolidation 8 weeks	Fluconazole 800 mg daily	Fluconazole: 6 mg/kg daily
3. Maintenance Until CD_4 count remains >200/15% for 6 months	Fluconazole 200 mg daily	Fluconazole 3 mg/kg/daily

INITIATE ART 4-6 WEEKS AFTER INITIATION OF ANTIFUNGAL THERAPY IN ART NAÏVE PATIENTS

* ***If amphotericin is not available for adults, use:*** Fluconazole 1200 mg daily for 2 weeks, followed by consolidation and maintenance treatment as above. *If amphotericin is not available for children – contact an HIV Specialist*

For patients with CD_4<100 cell/mL found to have positive cryptococcal antigen test: Evaluate for symptoms and signs of cryptococcal meningitis. If symptomatic perform LP and test for cryptococcal meningitis. If positive CSF (India ink or CRAG) treat as above. If asymptomatic or negative CSF, treat with oral fluconazole 1200mg for 2 weeks, followed by consolidation and maintenance treatment as above.

Special Considerations with ART

- Nevirapine levels are increased by nearly 100% with fluconazole administration. Switch NVP to DTG with high dose fluconazole co-administration, and discuss such cases with an HIV specialist.
- Patients on DTG can experience a 10-14% increase in serum creatinine, however no dose adjustment is required.
- There is no added toxicity with Tenofovir use and so TDF/FTC/EFV can be continued
- There is no need to discontinue EFV.

Fluconazole should be avoided in the first trimester of pregnancy or during breastfeeding. Discuss cases of women who develop cryptococcal meningitis during their first trimester of pregnancy with an HIV specialist

Management of Raised Intracranial Pressure

Cryptococcal meningitis is complicated by raised intracranial pressure (ICP) in over 50% of cases. Effective management of raised ICP is an essential part of treatment. LPs to check ICP should be performed routinely at baseline, on treatment days 3 and 7, and if any worsening symptoms occur. Drainage of CSF should be performed to normalize ICP to <20 cm H_2O.

Cryptococcal meningitis is uncommon among children. Given the lack of data in children, current recommendations for the treatment of cryptococcal meningitis are extrapolated from adult studies. Combination anti-fungal treatment appears superior to single agent therapy for the management of acute cryptococcal meningitis.

Discuss all pediatric cases with a Pediatric HIV Specialist.

8. Screening for Cervical Cancer

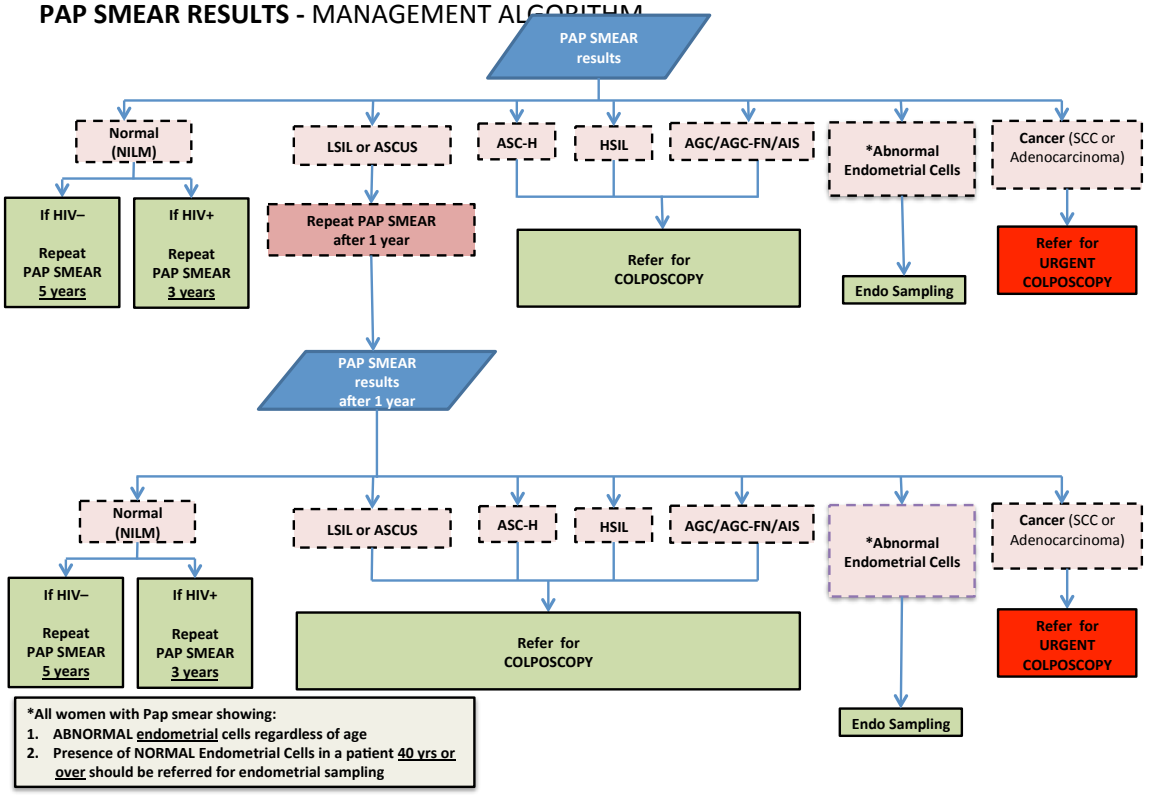
Screening criteria:

Screening age: 30 – 49 years

a. **Exception criteria: Recurrent STI/PV discharge with sexual debut >= 5 years**
   i. Women who fall outside of the screening age criteria may be referred for screening Pap smear at the discretion of medical doctors.
   ii. All patients who are **referred** for screening outside the inclusion criteria should have complete pelvic exam (bimanual and visualization of cervix via speculum exam) performed prior to referral, in keeping with thorough clinical evaluation and primary care norms whenever possible.
   iii. **Clinicians at screening centers should not send away patients who have been referred by clinicians (outside of the age range) *However, clinicians should discuss all such cases with HIV Women's Health Specialists.***

ALGORITHM #1

PAP SMEAR RESULTS - MANAGEMENT ALGORITHM



The Symptoms and Signs displayed in Table 9 below warrant pursuing a diagnosis as soon as possible, regardless of the age of a women. Any women who presents with these symptoms or signs must complete a pelvic exam (bimanual and visualization of cervix via speculum exam) and be referred for immediate biopsy and histology.

- If a cervical lesion is seen, a Pap smear or **VIA SHOULD NOT** be performed; instead an urgent biopsy should be done, and the patient must be referred to either the gynae oncology multidisciplinary clinic (PMH telephone: 3631630), or NRH Gynae OPD with histology results.
- If the facility has no biopsy capability, refer the patient to the nearest facility for an urgent biopsy.
- **Remember where there is clinical suspicion of cervical cancer, a definitive diagnosis needs to be made as quickly as possible, with urgent linkage to cancer treatment as soon as diagnosis is made.**

Table 9: Symptoms and Signs of Cervical Cancer

Early	Late	Very Late
Irregular bleeding **Post coital bleeding** **Post Menopausal bleeding** **Persistent vaginal discharge not responsive to standard STI syndromic management**	**Urinary frequency** **Backache** **Lower abdominal pains**	**Sever back pain** **Weight loss** **Decreased urine output** **Leakage of urine or faeces thru the vagina** **Swelling of lower limbs** **Breathlessness**

9. Revised Clinical Visit and Laboratory Monitoring Schedule

Tables 10 and 11 below outlines revised clinical visit scheduled for patient who have remained clinically stable with virologic suppression, <400 copies/mL for at least two years.

All health facilities that see HIV patients should adopt the new revised visit schedule (Tables 10 & 11) and laboratory requirements (Tables 12 and 13) for adults, adolescents and pediatrics.

Central Medical Stores will notify health facilities individually when they can begin to provide between 2-3 months ART stock to stable patients. Please do not begin to change pharmacy pick up schedule until your facility receives official notice to do so.

As long as patients remain clinically stable and virologically suppressed, they may continue to be placed on q 6-month appointments. However, once they become ill, default or experience virologic failure, they should resume clinic visits at the discretion of their physicians or return to the Year One clinic visit recommendations.

Table 10: CLINIC VISITS

YEAR ONE (stable and unstable patients)

Clinical Condition	1st Visit (Baseline)	Within 2 weeks	1 month	3 months	6 months	12 months	Q 6 months
Stable **Well with no co-morbidities & Suppressed**	**Confirm HIV status** **Baseline Labs** **Screen & Treat OIs** **Adherence Counseling**	**Initiate ART**	**X**	**X**	**X**	**X**	**X**
○ **All stable patients may be seen by ARV nurse prescriber** ○ Reviewed for toxicities & adherence ○ Screening for OI & TB at all visits ○ SRH services offered at all visits							
Clinical Condition	**1st Visit**	**Within 2 weeks of baseline screening**	**1 month**	**3 months**	**6 months**	**9 months**	**12 months**
Unstable: **CD4 <200** **Sick** **Co-morbidities** **Unsuppressed VL>400 copies/mL**	**Confirm HIV status** **Baseline Labs** **Screen & Treat OIs** **Adherence Counseling**	**Initiate ART**	**X**	**X**	**X**	**X**	**X**
○ **All unstable patients must be seen by MO** ○ Treated for illness & co-morbidities ○ After temporary illness resolved, unstable patients can be discharged from MO care to be seen by ARV nurse ○ Patients with co-morbidities or failing ART continue to be seen by MOs ○ SRH services offered at all visits ○ Once clinically stable, CD4 >200 and suppressed, patients may be seen as stable patients							

Table 11: CLINIC VISITS
Minimum Package of Care
AFTER YEAR ONE

Clinical Condition	**Month 12**	**Q6 thereafter**	
Stable Well with no co-morbidities & Suppressed	X	X	**Exception:** For adolescents 13-16 years Q 3
All stable patients may be seen by ARV nurse prescriber ○ Reviewed for toxicities & adherence ○ Screening for OI & TB at all visits ○ SRH services offered at all visits			
Clinical Condition	**Month 12**	**At the discretion of MO as necessary**	**Q3**
Unstable CD_4 <200 Sick Co-morbidities Unsuppressed	X	Pregnant Uncontrolled co-morbidities First Year on 2nd or 3rd Line Adherence issues	Stable co-morbidities Suppressed for one year on 2nd or 3rd line
○ **All unstable patients must be seen by MO** ○ Treated for illness & co-morbidities ○ After temporary illness resolved, unstable patients can be discharged from MO care to be seen by ARV nurse ○ Patients with co-morbidities or failing ART continue to be seen by MOs ○ SRH services offered at all visits			

Table 12: LABORATORY SCHEDULE – All Regimens

ADULTS AND ADOLESCENTS including Pregnancy

First Line

YEAR ONE	Baseline (or within 3 months prior)	1 month	3 months	6 months	12 months	Thereafter
VL	Only Pregnant Women**		X	X If not suppressed at 3 mos.	X	Q6 months
CD4	X		X	X If not >200	X	Q12 months
FBC	X				X	
Electrolytes	X					ACI*
AST/ALT	X		X			
GLUCOSE	X					
CR & CRCL	X	X	X	X	X	Q6 months on TDF
RPR***	X ANC					ACI

*ACI= as clinically indicated

** Pregnant Women VL Q3 during pregnancy or monthly until full suppression

*** RPR at 1st ANC visit and at 36 weeks gestation.

Second Line

All Regimens

YEAR ONE	At Switch	4-6 wks	3 months	6 months	12 months	Thereafter	
VL	If not within 3 months	X	X	X If not suppressed at 3 mos.	X	Q6 months, if clinically stable Otherwise Q4	
CD4	X		X	X If not >200	X	Q12 months	ACI
FBC	X				X		
Electrolytes	X					ACI	
AST/ALT	X		X				
RANDOM GLUCOSE			X				
CR & CRCL	X	X	X	X	X	Q6 months If on TDF	
RPR	X ANC					ACI	
CHOLES	X				X		

NOTE:

All patients with any of the following conditions should complete Total Cholesterol and Triglycerides every 6 months: HTN, DM, Obesity, 50 years of age and above.

Table 13: LABORATORY SCHEDULE: All Regimens

Infants & Children

First Line

YEAR ONE	Baseline (or within 3 months prior)	2 Weeks	1 months	3 months	6 months	9 months	12 months	Thereafter
VL	none			X	X	X	X	Q3 months
CD4 Count/%	X			X	X		X	Q6 months
FBC	X		X	X			X	Q12 months
Electrolytes	X							ACI
AST/ALT	X		X	X				
GLUCOSE	LPV/r only						LPV/r only	
Measure Growth & Development	X ANC	Weight only	Weight only	X	X	X	X	Q3 months

ACI= as clinically indicated

Pediatric Second Line

All Regimens

YEAR ONE	At Switch	6 wks	3 months	6 months	9 months	12 months	Thereafter
VL	If not done prior 3 months	X	X	X	X	X	Q3 months,
CD4			X	X If not >200		X	Q6 months
FBC	If not done in prior year	If switch to AZT	AZT only			X	Q12 months
Electrolytes							ACI
AST/ALT							
GLUCOSE TC/TG	X		X				
Measure Growth & Development	X	Wt only	X	X	X	X	Q3 months

Annex 1

Post-Exposure Prophylaxis (PEP) for Occupational Exposure to HIV

Ideally, PEP should be initiated within 1-4 hours of the incident, and at least within 72 hours of the exposure event.

PEP initiation should be based on a step-by-step protocol:

1. Determination of the HIV infectiousness of the body fluid to which the HCW was exposed and extent of exposure.
2. Immediate exposure management
3. HCW counseling and determination of the HCW's and source patient's HIV status
4. Decision whether or not to initiate PEP.
5. Initiation of PEP and monitoring of the HCW on PEP, including HIV testing of the exposed HCW after completion of PEP.

Body fluids and their HIV infectiousness:

Examples of infectious fluids include: blood, genital secretions, pericardial fluid, pleural fluid, synovial fluid, amniotic fluid, cerebral spinal fluid, ascitic fluid, breast milk, and any normally non-infectious fluid which is visibly contaminated with blood (or, in unusual cases, contaminated with any other infectious fluid).

- Fluids ***not infectious*** for HIV include: *urine, feces, tears, saliva, perspiration, sputum, pus from abscesses, and nasal secretions*, unless *visibly* contaminated with blood.

Exposure management:

- Wash exposed wounds and skin sites with soap and water.
- Flush mucous membranes with water.
- ***Avoid use of antiseptics, bleach, or other caustic agents***, including injection of exposed site with these agents.

HCW counseling and determination of HCW and source patient HIV status:

- If the HCW is found to be HIV-negative, then the HIV status of the source patient must be determined, unless the source patient is already known to be HIV-infected.
- If the source patient's HIV status is unknown, and if he refuses HIV testing, then an HIV rapid test will be obtained, however the results should not be shared with the source patient. If the source patient physically hinders or obstructs performance of rapid testing, then it is necessary to initiate PEP for the HCW.
- If the HCW is known to already be HIV-infected, PEP is not indicated, but HBV vaccination should be considered if the HCW has not already received it.
- To facilitate necessary evaluation and intervention, the rapid HIV test should be used if available. If the HCW refuses HIV testing, then PEP should not be given.
- If the HCW tests HIV-positive for the first time, then PEP is not indicated. However, necessary reassurance and emotional support should be provided to the HCW, with prompt referral for ART initiation.
- Include screening for Hepatitis B.

Exposures to fluids not normally infectious for HIV, as listed above, do not merit PEP, even if the source patient is HIV-positive. Remember, exposure to potentially HIV-infected fluids may or may not merit PEP.

ART Regimens for PEP

Once the decision to initiate PEP has been made, it should be started as soon as possible, ideally within 1-4 hours after exposure, but no later than 72 hours.

- For adolescents and adults:
  - **Initiate DTG/TRU or TDF/FTC/EFV** (whichever is immediately available)
  - **If side effects with EFV, switch to DTG as soon as possible**

- For children (follow pediatric dosing guides, as well as active involvement of family care-givers)

- Children <3 years begin PEP with **ABC/FTC/NVP**
  Children >3 years <35 kgs begin PEP with **ABC/3TC/EFV**
  Children >35 kgs begin PEP with **DTG/TRU**

- Assure that the HCW or caregivers understands the importance of completing the entire 1-month regimen.
- Schedule clinical follow-up 2 weeks after PEP initiation, both for evaluation for possible side effects and to provide adherence counseling and emotional support.
- Monitor laboratories of HCWs on PEP based on the patient's medical history.
- In some cases, baseline and follow-up laboratory testing are not necessary. However**, obtaining any baseline laboratory tests must not delay initiation of PEP beyond 4 hours of the incident.**
- Pregnancy is not a contraindication to PEP.
- Counsel HCW to practice safe sex during the period of PEP and until repeat HIV testing.
- Women who are breastfeeding must be counseled regarding the risks of breastfeeding following an HIV exposure and should be advised to abstain from breastfeeding.

Repeat HIV testing of HCW after PEP:

- The HCW should return for repeat HIV testing at 4 weeks, 3 months, and 6 months after the initial exposure.

1.4.2 PEP and Other Indicated Care for Victims of Sexual Violence

Victims of rape, sodomy, and defilement – including infants and children - must be brought to the hospital or clinic for PEP evaluation first, before a detailed police interrogation is initiated. It is essential that police understand that PEP must be started immediately (within 72 hours) for all victims of sexual violence.

- Follow the PEP protocol for all such victims, including infants and children, exactly as outlined above for HCWs.
- Clinical treatment for rape, including care for genital/rectal trauma must not delay prompt initiation of PEP.
- Even if the rapist tests HIV-negative, the result must be interpreted with caution, because of the risk that the rapist is in the "window period."
- **The practitioner must not wait for a police report before initiating PEP, nor should they be bound by any police report in determining the need for PEP**.
- A patient history of violent penetrative sex is sufficient for initiating PEP, per the above protocol. Although *not* a requirement for initiation of PEP, the victim should be encouraged to report the rape to the police, once PEP has been initiated.
- Victims of sexual violence, especially children, require special care, both medical and psychosocial.

Although appropriate referrals for psychosocial care may be necessary, the treating clinician must also provide such care, regardless of whether or not the victim receives PEP, as follows:

- Screening for STIs that may have been transmitted during the rape should be done by obtaining cultures for Chlamydia and Gonorrhea, if available, as well as baseline and follow-up RPR.
- After obtaining screening pregnancy test, consideration should be given to offering emergency contraception to prevent pregnancy.
- The patient/caregiver should receive education about signs and symptoms of STIs, including the importance of ongoing safe sex for adult victims.
- If genital/rectal trauma has occurred, promptly refer the patient for appropriate surgical, urological, or gynecological care, as indicated.
- Depression, shame, guilt, and suicide often followed sexual violence, and ongoing psychosocial interventions and counseling are required, including social worker referral for psychiatric evaluation.

ANNEX 2

The World Health Organization's approach to assessing a patient's medical eligibility for contraceptive method in the context of HIV risk and infection provides a useful clinical framework; it is called the WHO Medical Eligibility Criteria (MEC) (World Health Organization Medical Eligibility Criteria for Contraceptive Use, 5th Edition (2015). The Botswana National Family Planning Programme utilizes the WHO MEC approach. In the case of MEC category 3 and 4, HIV and contraception clients can be referred to a contraceptive specialist for further advice.

In the MEC classification system, there are 4categories:

1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition which represents an unacceptable health risk if the contraceptive method is used

CATEGORY	WITH CLINICAL JUDGEMENT	WITH LIMITED CLINICAL JUDGEMENT
1	Use method in any circumstances	**Yes** (Use the method)
2	Generally use the method	
3	Use of method not usually recommended unless other more appropriate methods are not available or not acceptable	**No** (Do not use the method)
4	Method not to be used	

Summary of contraceptive methods and ART/TB drugs according to the WHO MEC for Contraceptive Use and the WHO Guidance Statement for hormonal contraceptive methods for women at high risk of HIV and living with HIV (2014)

	CHC	POP	Progestin-only injectables	Progestin-only implants	Copper IUD I	Copper IUD C	LNG IUS I	LNG IUS C
Nucleoside reverse transcriptase inhibitors (NRTIs) ABC, TDF, AZT, 3TC, DDI, FTC, D4T	1	1	DMPA=1	1			2/3	2
Non-Nucleoside reverse transcriptase inhibitors (NNRTIs)								
Efavirenz and Nevirapine	2	2	DMPA=1	2			2/3	2
Etravirine and Rilpivirine	1	1	DMPA=1	1			2/3	2
Raltegravir (Integrase inhibitor)	1	1	DMPA=1	1			2/3	2
Protease inhibitors ATV/r, LPV/r, DRV/r, RTV	2	2	DMPA=1	2			2/3	2
Rifampicin or rifabutin for TB	3	3	DMPA=1	2				

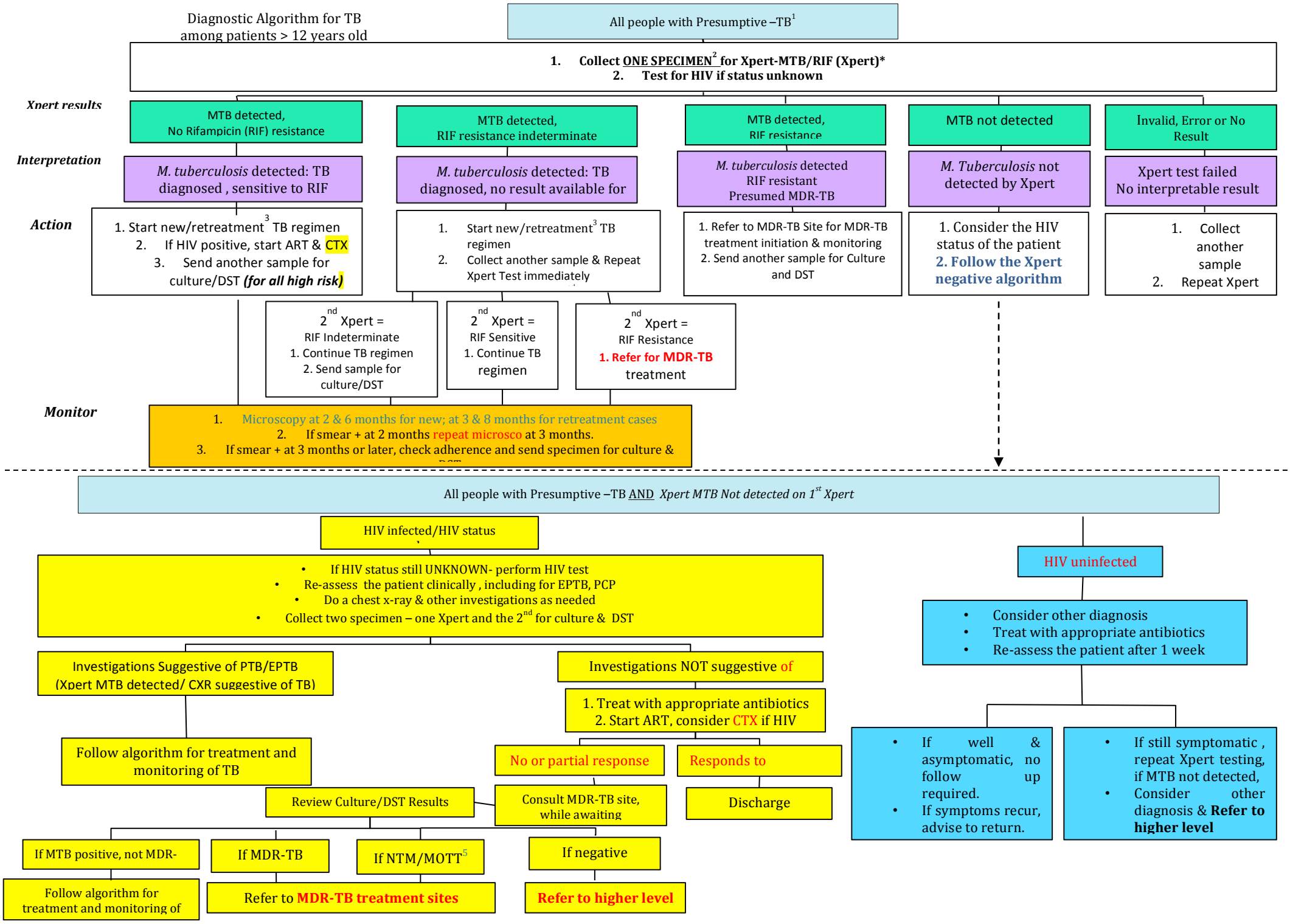
ANNEX 3

Information Regarding Dolutegravir (DTG)
(also known by brand name of TIVICAY)

DTG is an HIV Type 1 (HIV-1) Integrase strand transfer inhibitor (INSTI) that can be used in adults and children 12 years and older who weigh more than 40kg in combination with other anti-retroviral medications for the treatment of HIV. Integrase inhibitors block HIV replication by preventing the viral DNA from integrating into the genetic material of human immune cells (T-cells). This step is essential in the HIV replication cycle and is also responsible for establishing chronic infection. Dolutegravir is approved for use in over 90 countries across North America, Europe, Asia, Australia, Africa and Latin America.

Additional information regarding DTG includes:

- May be taken without regard to food
- **The most commonly reported ADR include insomnia (3%), fatigue (2%), and headache (2%)**.
- Hypersensitivity reactions characterized by rash, constitutional findings, and sometimes organ dysfunction, including liver injury, have been reported (in <1% or fewer patients). It is contraindicated in patients with previous history of hypersensitivity. Discontinue DTG immediately if signs of hypersensitivity develop.
- **DTG inhibits OCT2 and MATE1, which are responsible for tubular secretion of creatinine resulting mild increase in creatinine after initiation, which remains stable.** No DTG dose adjustment is necessary in INI-naïve subjects with mild, moderate or severe renal impairment.
- **Drugs that are metabolic inducers may decrease the plasma concentrations of DTG, e.g. ATT.**
- **Take DTG 2 hours before or 6 hours after taking cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium or buffered medications.** Alternatively, DTG and supplements containing calcium or iron can be taken together with food.
- **Co-administration of DTG with dofetilide (an antiarrhythmic) is not recommended**
- Plasma concentrations of metformin increase with co-administration of DTG. **Metformin** requires a total daily dose limit of 1,000mg with co-administration. When stopping DTG, metformin dose may require an adjustment. Discuss w HIV Specialist
- **Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of DTG**. Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with DTG is recommended in patients with underlying hepatic disease such as hepatitis B or C.
- Redistribution/accumulation of body fat and immune reconstitution syndrome have been reported in patients treated with combination antiretroviral therapy.
- **The efficacy of DTG 50 mg is reduced in patients with an INSTI-resistance** Q148 substitution plus 2 or more additional INSTI-resistance substitutions including T66A, L74I/M, E138A/K/T, G140S/A/C, Y143R/C/H, E157Q, G163S/E/K/Q, or G193E/R.
- **Dolutegravir in Pregnancy**
  DTG is classified as a B1 by FDA: *Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have also not shown evidence of an increased occurrence of fetal damage.*


Diagnostic Algorithm for TB among patients > 12 years old
All people with Presumptive –TB[1]
1. Collect ONE SPECIMEN[2] for Xpert-MTB/RIF (Xpert)*
2. Test for HIV if status unknown
Xpert results
MTB detected, No Rifampicin (RIF) resistance
MTB detected, RIF resistance indeterminate
MTB detected, RIF resistance
MTB not detected
Invalid, Error or No Result
Interpretation
M. tuberculosis detected: TB diagnosed , sensitive to RIF
M. tuberculosis detected: TB diagnosed, no result available for
M. tuberculosis detected RIF resistant Presumed MDR-TB
M. Tuberculosis not detected by Xpert
Xpert test failed No interpretable result
Action
1. Start new/retreatment[3] TB regimen
2. If HIV positive, start ART & CTX
3. Send another sample for culture/DST (for all high risk)
1. Start new/retreatment[3] TB regimen
2. Collect another sample & Repeat Xpert Test immediately
1. Refer to MDR-TB Site for MDR-TB treatment initiation & monitoring
2. Send another sample for Culture and DST
1. Consider the HIV status of the patient
2. Follow the Xpert negative algorithm
1. Collect another sample
2. Repeat Xpert
2nd Xpert = RIF Indeterminate
1. Continue TB regimen
2. Send sample for culture/DST
2nd Xpert = RIF Sensitive
1. Continue TB regimen
2nd Xpert = RIF Resistance
1. Refer for MDR-TB treatment
Monitor
1. Microscopy at 2 & 6 months for new; at 3 & 8 months for retreatment cases
2. If smear + at 2 months repeat microsco at 3 months.
3. If smear + at 3 months or later, check adherence and send specimen for culture &
All people with Presumptive –TB AND Xpert MTB Not detected on 1st Xpert
HIV infected/HIV status
• If HIV status still UNKNOWN- perform HIV test
• Re-assess the patient clinically , including for EPTB, PCP
• Do a chest x-ray & other investigations as needed
• Collect two specimen – one Xpert and the 2nd for culture & DST
HIV uninfected
• Consider other diagnosis
• Treat with appropriate antibiotics
• Re-assess the patient after 1 week
Investigations Suggestive of PTB/EPTB (Xpert MTB detected/ CXR suggestive of TB)
Investigations NOT suggestive of
1. Treat with appropriate antibiotics
2. Start ART, consider CTX if HIV
• If well & asymptomatic, no follow up required.
• If symptoms recur, advise to return.
• If still symptomatic , repeat Xpert testing, if MTB not detected,
• Consider other diagnosis & Refer to higher level
Follow algorithm for treatment and monitoring of TB
No or partial response
Responds to
Discharge
Review Culture/DST Results
Consult MDR-TB site, while awaiting
If MTB positive, not MDR-
If MDR-TB
If NTM/MOTT[5]
If negative
Follow algorithm for treatment and monitoring of
Refer to MDR-TB treatment sites
Refer to higher level

NOTES TO ADULT & ADOLESCENT TB DIAGNOSTIC ALGORITHM

Adults and >12 Years

1. Presumptive TB criteria: a) If HIV infected /unknown – any one symptom of cough, fever, night sweat and weight loss of **any duration;** b) If HIV uninfected: - cough, fever night sweat and weight loss for **2 weeks**
2. Spontaneous or induced sputum, gastric lavage, lymph node fine needle aspirate, pleural biopsy or cerebrospinal fluid (CSF). If the specimen is pleural fluid, send for culture and DST not for Xpert. If the specimen is bloody, please repeat the sample, Xpert cannot be performed on bloody samples.
3. **High risk:** MDR-TB Contact, Previously treated TB, Health Care Worker (including laboratorians, cleaners and drivers)

NOTES TO THE PEDIATRIC TB DIAGNOSTIC ALGORITHM

1. Follow Weights on growth charts; Note higher levels of EPTB TB in children if presenting with other clinical symptoms. This may require testing of other samples (e.g. CSF/ascites/pleural fluid/biopsy).
2. **IMCI Danger signs:** Lethargy, unconscious, inability to feed or breastfeed, vomiting.
3. **TST - Refer to annex 4 for details of performing TST.**
4. **GeneXpert:** If specimen is pleural fluid, send for culture and DST not for geneXpert. If specimen is bloody, please repeat the sample. GeneXpert cannot be performed on a bloody sample.
5. Bacterial confirmation should always be saught but is not essential before starting ATT. If child cannot produce sputum, collect 2 gastric aspirates or 2 induced sputum samples for MTB Xpert and culture. **(Refer to annex 5 for details on gastric aspirates and sputum induction).**
6. CXR findings suggestive of TB include any one of the following: Hilar adenopathy, infiltrates, airway compression, pericardial effusion, pleural effusion
7. Remember: Infants are at extremely high risk for TB following documented exposure. Symptomatic children under 5 years old should be preferably be assessed by a doctor.

Algorithm to Diagnose PTB & TB Lymphadenitis* TB in Children ≤12 years

Suspect TB if there ≥ two of the following[1]:

- History of recent TB contact (past year)
- Cough ≥ 2 weeks
- Fever ≥ 2 weeks
- Failure to thrive (weight loss or no weight gain in 3 months)
- Fatigue or reduced playfulness ≥ 2 weeks
- Enlarged lymph nodes (greater than 1x1cm) ≥ 2 weeks

Danger signs (-)

[2]Danger signs (+)

Follow IMCI

If Presumptive TB

EVALUATE FOR TB
HIV test if not done
TST[3]
2 sputum samples/lymph node aspirates or 2 Gastric Aspirates
(1 for Xpert[4] & 1 for culture)[5]
CXR- PA and Lateral

REEVALUATE

- If **TB contact start ATT** +
- If **no TB contact** refer to higher level care for further evaluation
- Consider repeat TB testing including MTB Expert if TB likely

TST (+) or AFB/Xpert/culture (+) or CXR[6] suggests TB

TST (-) AFB/Xpert/culture (-) and CXR[6] does not suggest TB

Treat for TB+
HIV (+) - ensure ART and CPT

Give 1 week of antibiotics for bacterial infection and follow up in 7-10 days and consider other diagnoses e.g malnutrition if FTT

No response or Partial response[7]

Good Response

If child has a TB contact- initiate IPT if < 5 years or if HIV (+) up to age 12

Discharge

HIV care

MTB EXPERT RESULTS

MTB detected/No rifampicin resistance

- Start new TB regimen if no TB treatment history
- Start retreatment TB regimen if history of TB treatment and follow up culture results
- Follow up culture/DST results especially if high risk for drug resistance (e.g. contact)

MTB detected/Rif resistance indeterminate

- Send another sample for repeat Xpert
- While waiting start new or retreatment TB regimen
- If Xpert remains indeterminate send another sample for LPA, Culture and DST

MTB detected/ Rif resistance detected

- Refer to MDR-TB Site for MDR-TB treatment initiation
- Follow sample sent for culture & DST and request LPA on sample

MTB Not Detected

- Consider other results and follow algorithm as indicated

Invalid/ error

- Collect another sample
- Repeat Xpert
- If the specimen is pleural fluid, send for culture and DST not for geneXpert
- If the specimen is bloody, please repeat the sample, Xpert cannot be performed on bloody samples.

If child is MDR contact or culture suggests resistance – refer to MDR TB site for treatment

+ MDR Contact or Culture with Resistance

ANNEX 5

List of Clinical Care Specialists

PECIALIST PANEL

Adult and General HIV/AIDS and TB care:

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**** Denotes HIV Resistance Specialists***

^ Denotes HIV & TB Specialists

ANNEX 6

ARV Nurse Dispensers and Prescribers Information.

Anyone who does not meet the general, clinical and laboratory criteria For ARV Nurse Initiation MUST BE INITIATED BY a doctor.

Adult ARV Eligibility Criteria for ARV Nurse Initiation:

General:

- CD_4 count: >150 cells/ml
- Appears well and is ambulatory
- Self reports no significant medical issues
- No WHO 2,3,4 conditions
- No previous history of receiving sdNVP during labour

Clinical Criteria:

There should be NONE of the following conditions:

- rash involving mucous membranes
- shortness of breath or tachycardia
- unintentional weight loss > 10% baseline weight
- cough or fever or night sweats
- significant cervical lymphadenopathy
- previous history of seizures, altered mental status
- neurological deficits
- nausea, vomiting or diarrhea
- dehydration
- Jaundice or enlarged liver
- headaches, blurred vision
- abnormal pap smear
- abdominal pain with tenderness, rebound or guarding on examination
- severe depression or suicide

Laboratory Criteria:

- Hemoglobin > 7 g/dL
- Platelets >150 x 109/L
- Total WBC > 1000 /mL
- ALT/AST: Within Normal Limits
- Glucose < 7 mmol/L
- Creatinine <120 umol/L
- Creatinine Clearance ≥ 60 cc/min

2012 Standard Adult 1st Line Regimen

Men	Atripla	1 tab PO Q nocte x (time until next refill)
Women	Atripla	1 tab PO nocte x (time until next refill)

2008 Standard Adult 1st Line Regimen

(Stable follow up. Note: both men and women may be found to be taking either CBV or EFV, there is no dosage change based on gender)

Men	CBV, EFV	CBV 1 tab PO BD x (time until next refill) EFV 600 mg PO Q nocte x (time until next refill)

Women (of Child bearing age)	CBV/NVP	CBV 1 tab PO BD x (time until next refill) NVP 200 mg PO BD x (time until next refill)

Adult Cotrimaxazole Prophylaxis
For women and men with CD4 counts <200 cells/ml:
Cotimaxazole 2 tabs PO OD until CD4 >200 for three months
(2 tabs of 480mg single strength=960mg OD)
For cotrimaxazole allergy or intolerance use:
Dapsone 100 mg PO OD until CD4 > 200 for three months

Discuss Sexual Health Reproductive Health with all patients:
- Inquire about their partner(s) and children HIV status: TEST or refer for testing
- Inquire about their current contraceptive method: prescribe or refer for prescription
- Inquire about date of last menstrual period. If pregnancy suspected send for pregnancy test; if positive initiate as soon as possible.
- Inquire about history or current STIs, refer for treatment if necessary

Complete a full physical exam for ALL patients, as follows:
General Appearance/condition: age, cognition, breathing, ambulatory status state of nutrition, pale, sweating, dehydrated, fever
Vital Signs: weight, temperature, pulse, BP, respirations
Skin: jaundice, rashes, eruptions, ulcerations
CNS: confusion, speech, balance
Head: deformities, masses, evidence of trauma
Ears: Hearing, external canals, discharge, cerumen, tympanic membrane
Eyes: sclera, visual acuity, corneal reflex, movements intact
Nose & Paranasal sinuses: rhinorrhea, frontal, mastoid, maxillary tenderness
Mouth: thrush, dentition, condition of gums, lip fissures
Neck: rigidity, thyroid, cervical lymph nodes
Axilla: lymph nodes, ulcerations
Chest: cough, SOB, wheezes, rhonci, rales,consolidation
Heart: RRR, murmurs
Abdomen: tenderness, guarding, masses, bowel sounds
Genitals: lymph nodes, ulcerations, PV d/c
Extremities: peripheral neuropathy, edema, lesions

Remember: All patients found to have significant physical findings must be initiated by a doctor

Side Effects Attributable to ART:
CNS effects (insomnia, nightmares, dizziness, headache): EFV
Rash (mild to severe): NVP
Anemia, neutropenia, weakness, fatigue: CBV
Renal Insufficiency, headache, nausea, vomiting: TDF
GI intolerance, nausea, vomiting, diarrhea: LPV/r
Headache, insomnia, fatigue, rash: DTG

ANNEX 7
LIST OF ABREVIATIONS

>, <	greater than, less than
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATT	anti-tuberculosis therapy
ART	antiretroviral therapy
BD	twice a day
BNTP	Botswana National Tuberculosis Programme
CSF	cerebral spinal fluid
CSW	commercial sex worker
CTX	cotrimoxazole
CrCl	creatinine clearance
DBS	dried blood spot
DS	"double-strength" CTX (= 2 "single-strength" CTX)
DNA PCR DNA	polymerase chain reaction
E	ethambutol
ELISA	Enzyme-linked immunosorbent assay
FBC	full blood count
FDCs	fixed-dose combinations
H	isoniazid
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCW	healthcare worker
Hgb	hemoglobin
HIV	human immunodeficiency virus, type 1 (HIV-1)
HIV-DR	HIV drug resistance
ICP	intracranial pressure
INH	isoniazid
IPT	isoniazid preventive therapy
IRIS	immune reconstitution inflammatory syndrome
IV	intravenous
IVIG	intravenous immunoglobulin
kg	kilogram
KS	Kaposi sarcoma
LEEP	loop electrosurgical excision procedure
LP	lumbar puncture (spinal tap)
MAC	mycobacterium avium complex
mg	milligram
mL	milliliter
mmol	millimole
mos	months
MDR-TB	multidrug-resistant tuberculosis
MOH	Botswana Ministry of Health
MSM	men who have sex with men
MTCT	mother-to-child transmission (of HIV)
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
OD	once daily
OI	opportunistic infection
PEP	post-exposure prophylaxis
PI	protease inhibitor

PMTCT	prevention of mother-to-child transmission (of HIV)
po	by mouth, orally
PrEP	pre-expose prophylaxis
q	every, e.g., q3hours= every 3 hours
R	rifampicin
RBT	rifabutin
RFP	rifapentine
sd-NVP	single-dose nevirapine
SMC	safe male circumcision
STI	sexually transmitted infection
SS	single-strength CTX (TMP 80mg/SMX 400mg)
TAM	thymidine analogue mutation
TB	*mycobacterium* tuberculosis
TDS	three times a day
TC	total cholesterol
TG	triglycerides
TMP	trimethoprim
ULN	upper limit of normal
VL	viral load
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis
Z	pyrazinamide

Anti-Retroviral Abbreviations:

ATA	atazanavir
ATA/r	atazanvir coformulated with ritonaivr
AZT	zidovudine, ZDV
3TC	lamivudine
CBV	combivir
FTC	emtricitabine
DTG	dolutegravir
DAR	darunavir
ABC	abacavir
TDF	tenofovir
NVP	nevirapine
EFV	efavirenz
LPV/r	ritonavir-boosted lopinavir ["Kaletra," "Aluvia"]
SQV	saquinavir
RAL	raltegravir
RTV	ritonavir
r	low dose ritonavir, used as a "booster")