REPUBLIC OF BOTSWANA
Ministry of Health

THE BOTSWANA 2023 INTEGRATED HIV CLINICAL CARE GUIDELINES

DIVISION OF HIV/AIDS PREVENTION AND CARE

Masa Antiretroviral Therapy

Treat ALL

FOREWORD

The Results of the Fifth Botswana AIDS Impact Survey (BAIS V) and the 2023 Botswana UNAIDS HIV Estimates, documenting Botswana's achievements in the fight against HIV are important milestones to be celebrated. These milestones should catalyze and reinvigorate our efforts towards reaching HIV epidemiologic control and finally ending the Era of AIDS in Botswana after decades of struggle. While the human, financial and personal investment in this battle has been great, we must remember that our goals were realized through our collective efforts towards improving the lives of those we serve.

Now as we pivot towards facing new healthcare challenges, there has never been a more important time to reflect on the lessons learned from HIV and build upon our primary healthcare systems, to address rising comorbidities and prevent mortality. To further optimize HIV clinical care, we must continue to stop the spread of HIV among youth, provide appropriate public health interventions to key populations and streamline routine service delivery. Fundamental to these emerging goals is strengthening our healthcare systems to provide rights-based integrated and comprehensive healthcare services to all People Living with HIV, their families and communities.

Having achieved what many believed was unachievable in our battle against HIV provides enduring hope that meeting our emerging health challenges is not only possible, but well within our reach. And as before, our ability to address Sexual Reproductive Health issues, Non-Communicable Diseases and other Infectious Disease epidemics, will depend on our resolve to work in unity across all cadres of healthcare providers, academics and development partners to save more lives.

The 2023 HIV Integrated Clinical Care Guidelines will undoubtedly move us closer to solving emerging public health challenges, while maintaining our successes against HIV and ensuring that every PLHIV's longevity and quality of life are guaranteed.

Signature:.....

Permanent Secretary Of the Ministry of Health
Prof. Oathokwa Nkomazana

Acknowledgements & Appreciation by Ms. Dinah Ramaabya & Dr. Bornapate Nkomo

Great appreciation is due to all healthcare professionals that undertook countless hours of deliberations over the past two years to develop the revised 2023 HIV Clinical Care Guidelines. The expanded recommendations present the latest in optimized HIV care and support an integrated approach to the diagnosis and treatment of cardiovascular and metabolic dysfunction, hepatitis, tuberculosis, opportunistic infections and other comorbidities - more comprehensively than ever before.

New 4th Generation HIV testing algorithms aim to improve testing accuracy and reduce the HIV window period time. Routine testing of all pregnant women for HIV, Viral Hepatitis and Syphilis, as well as birth testing for high-risk HIV exposed infants, will reduce congenital disease transmission and improve mother and infant treatment and care. Transitions to dual therapy for stable patients on ART will decrease toxicities, particularly rising renal insufficiency and metabolic disorders seen with the use of older ART regimens. Expanded sections on Opportunistic Infections and Sexually Transmitted Infections will assist in providing fully integrated care at every health care facility. A much-needed focus on the diagnosis and treatment of Viral Hepatitis will also move us forward toward its elimination.

Keeping PLHIV alive, healthy and thriving are the key objectives of the 2023 HIV Integrated Clinical Care Guidelines. In addition to the members of the 2022-2025 HIV Clinical Care Guidelines Committee, we sincerely thank the following individuals who were instrumental in seeing these Guidelines to completion: Deputy Permanent Secretary of Health, Dr. Tshepo Machacha, Guidelines Committee Chair - Dr. Tendani Gaolathe, Dr. Max Kapanda, Principal Medical Officer of the National ART Programme, Dr. Lynn Tjirare of the National ART Programme, Drs. Mogomotso Matshaba & John Farirai of Botswana-Baylor, Dr. Ndwapi Ndwapi of BUMMHI, Dr. Malviya Alankar, Dr. Gang Sun & Ms. Mpho Mmelesi of UNAIDS, Dr. Tebogo Madidimalo of the WHO, Dr. Steven Hong and Dr. Mpho Letebele of CDC-PEPFAR, Dr. Roger Shapiro and Dr. Gbolahan Ajibola of BHP, Mr. Justus Ogando & Ms. Ana Moore of CHAI, Mr. Ashenafi Hordofa of GHSC-PSM, Mr. Pono Pono of BOMRA, Community representative and tireless HIV Activist – Mr. Stanley Monageng, Dr. Ava Avalos, Guidelines Senior Editor and MoH HIV Technical Advisor. And finally, the remarkable and legendary Dr. Diana Dickinson of Independence Surgery who generously contributed her time, wealth of clinical expertise and fierce HIV activism.

Sincere Thanks & May Our Collective Efforts Save Lives and Reduce Suffering.

On to the New.....
2023 Optimization and Improvement in HIV Treatment, Care & Support

- **Introduction of two-drug regimens (3TC+DTG) in clinically stable adults** taking anti-retroviral therapy (ART) will reduce long term toxicities and decrease costs overall. Numerous clinical trials have now shown that switching to dual therapy ART is non-inferior, well tolerated and less toxic. Dual therapy will benefit all eligible patients, particularly those who have been on ART for many years with numerous co-morbidities.

- **Routine use of Darunavir/Ritonavir (DAR/r) and Doravirine (DOR)** for second line treatment regimens and **Doravirine** for those with Dolutegravir (DTG) intolerance.

- **New definition of viral load suppression to <200 copies/mL** to improve clinical outcomes and decrease the development of HIV drug resistance.

- **Improved ART Treatment Failure Management** with the introduction of Directly Observed Therapy (DOT) for those with confirmed virologic failure.

- **New Section on the diagnosis and management of Hepatitis/HIV co-infection.**

- **Expanded Testing Algorithms for HIV, Hepatitis and Syphilis** for all pregnant women and the introduction of birth testing for all HIV exposed infants.

- **Improvement of care for PLHIV with liver disease** with improved diagnostic algorithms of Hepatitis B and C, Non-Fatty Liver Disease (NFLD) and treatment for Hepatitis C.

- **Revised & expanded Algorithms for cervical cancer screening & treatment.**

- **Endorsement of the use of Long-Acting Injectables** with injectable Cabotegravir for PrEP and injectable Cabotegravir and Rilpivirine for ART treatment, to improve the lives of PLHIV and their treatment outcomes. Implementation dates will depend upon the determination of cost effectiveness and product availability within specific HIV populations.

- **Introduction of PrEP in pregnancy and breastfeeding** for HIV-negative women at high risk for HIV infection, beginning with oral formulations until the use of long-acting injectables becomes available.

- **Expanded access to PEP.**

- **Endorsement of shorter courses of anti-tuberculous therapy (ATT)** for both drug sensitive and multidrug resistance TB for adults (and adolescents) to improve adherence, treatment outcomes and decrease toxicities. Implementation is scheduled to begin before the end of 2023.

- **Focus on Wellness** – Moving beyond HIV suppression, recommendations on lifestyle modifications such as routine exercise, improved nutrition, safer sexual encounters, reducing alcohol use and smoking cessation, which form the true cornerstones of ensuring longevity for PLHIV are highly encouraged and recommended.

- **Increased focus to improve care of HIV aging populations and those who are fragile**.

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International and National HIV/AIDS Resource Directory

RELEVANT HIV/AIDS WEBSITES

EACS Guidelines - European AIDS Clinical Society.
Available at: https://www.eacsociety.org/guidelines/eacs-guidelines/

DHHS (Department of Health Services) HIV/AIDS Treatment Guidelines | Clinicalinfo.HIV.gov (2023). Available at: https://clinicalinfo.hiv.gov/en/guidelines/

CDC (Center for Disease Control) HIV/AIDS Guidelines and Recommendations
Available at: https://www.cdc.gov/hiv/guidelines/index.html/

SAHCS South African HIV Clinicians Society
Available at: https://sahivsoc.org/Subheader/Index/sahcs-guidelines/

CCO (Clinical Care Options) Free HIV CE and HIV CME for Healthcare Professionals |
Available at: https://clinicaloptions.com/CE-CME/hiv/

ITPC Global (International Treatment Preparedness Coalition (2021)
Home - ITPC Global. Available at: https://itpcglobal.org/

i-Base HIV Guidelines.
Available at: https://i-base.info/guides/

NAM. aidsmap. National AIDS Manual. UK
Available at: https://www.aidsmap.com/

University of Liverpool – HIV Drug Interactions Website
Available at: https://www.hiv-druginteractions.org/

BOTSWANA-BASED ORGANIZATIONS & WEBSITES

ACHAP - African Comprehensive HIV & AIDS Partnership
Available at: http://www.achap.org/

BOFWA - Botswana Family Welfare Association.
Available at: https://bofwa.org.bw/

Bonela - The Botswana Network on Ethics, Law and HIV/AIDS.
Available at: https://bonela.org/

BOSASNet - Botswana Substance Abuse Support Network.
Available at: http://bosasnet.com/

BOCHAIP - Botswana Christian Health & AIDS Intervention Program (BOCHAIP).
Available at: https://www.bochaip.org.bw/

BHP - Botswana Harvard AIDS Institute Partnership for HIV Research & Education.
Available at: https://www.bhp.org.bw/

Botswana Baylor Children's Centre of Excellence.
Available at: https://baylorbotswana.org.bw/

BUMMHI - Botswana University of Maryland School of Medicine Health Initiative.
Available at: https://bummhi.business.site/

Tebelopele Voluntary Testing and Counselling
Available at: https://tebelopele.org.bw/

LIST OF ABBREVIATIONS

>, <	Greater than, less than
3HP	Isoniazid and Rifapentine
AA	Alcoholics Anonymous
ACE	Angiotensin-Converting Enzyme
ADR	Adverse Drug Reaction
AEs	Adverse Events
AFB	Acid Fast Bacilli
AHC	Advanced HIV Care
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Aminotransferase
ANC	Antenatal Care
ARB	Angiotensin Receptor Blockers
ART	Antiretroviral Therapy
AST	Aspartate Aminotransferase
ATT	Anti-Tuberculosis Therapy
BD	Twice a Day
BP	Blood Pressure
BPaLM	Bedaqualine, Pretomonid, Linezolid, Moxifloxacin
BSA	Body Surface Area
BV	Bacterial Vaginosis
CA	Cancer
CAD	Coronary Artery Disease
CCB	Calcium Channel Blockers
CD4	Cluster Designation 4
CKD	Chronic Kidney Disease
CMV	Cytomegalovirus
CNS	Central Nervous System
COCs	Combined Oral Contraceptive Pills
COVID-19	SARS COVID-19
CrAg	Serum Cryptococcal Antigen
CrCl	Creatinine Clearance
CSF	Cerebrospinal Fluid Analysis
CT	Computed Tomography
CTX	Cotrimoxazole
Cu IUD	Copper Intrauterine Device
CPAC	Comprehensive Post-Abortion Care
CVD	Cardiovascular Disease
CVS	Cardiovascular
CWC	Child Welfare Clinics
DAA	Direct Acting Antiviral
DBS	Dried Blood Spot
DDI	Drug-Drug Interactions
DHIS	District Health Information System
DM	Diabetes Mellitus
DMPA	Depot-Medroxyprogesterone Acetate
DNA	Deoxyribonucleic Acid
DOT	Directly Observed Therapy
DR	Drug Resistance
DS	Drug Sensitive
DST	Drug Sensitivity Testing
eGFR	Estimated Glomerular Filtration Rate
EC	Emergency Contraceptive
ECP	Emergency Contraceptive Pills
EPTB	Extra Pulmonary Tuberculosis
FBC	Full Blood Count
FDC	Fixed Dose Combination
GBV	Gender Based Violence
GFR	Glomerular Filtration Rate
GI	Gastrointestinal
GTT	Glucose Tolerance Test

HBcAb	Hepatitis B Core Antibody
HBsAb	Hepatitis B Surface Antibody
HBVsAg+	Hepatitis B Surface Antigen Positive
HCV	Hepatitis C Virus
HCVAb	Hepatitis C Antibody
HCC	Hepatocellular Carcinoma
HCTZ	Hydrochlorothiazide
HDV	Hepatitis D Virus
HEP B	Hepatitis B Virus
HIV	Human Immunodeficiency Virus
HIV-DR	HIV Drug Resistance
Hgb	Hemoglobin
HgbA1C	Hemoglobin A1C
HMOD	Hypertension-Mediated Organ Damage
HRT	Hormone Replacement Therapy
HSV	Herpes Simplex Virus
HPTN	HIV Prevention Trials Network
HPV	Human Papilloma Virus
HTE	Highly Treatment Experienced
HTN	Hypertension
ICF	Intensified Case Finding
ICP	Increased Intracranial Pressure
IDCC	Infectious Disease Care Clinic
INH	Isoniazid
INSTI-N	Integrase Naïve
IPT	Isoniazid Preventive Therapy
IPV	Intimate Partner Violence
IRIS	Immune Reconstitution Inflammatory Syndrome
IV	Intravenous
KCL	Potassium Chloride
KS	Kaposi's Sarcoma
LAM	Lipoarabinomannan
LARC	Long-Acting Reversible Contraception
LDL	Low-Density Lipoprotein
LEEP	Loop Electrosurgical Excision Procedure
LFA	Lateral Flow Assays
LF-LAM	Lateral Flow Urine Lipoarabinomannan
LFTs	Liver Function Tests
LNG UID	Levonorgestrel Intrauterine Device
LP	Lumbar Puncture
LTFU	Lost to Follow Up
LVH	Left Ventricular Hypertrophy
MAC	Mycobacterium Avium Complex
MCS	Microscopy, Culture and Sensitivity
MD	Medical Doctor
MEC	Medical Eligibility Criteria
MDR-TB	Multidrug Resistant Tuberculosis
Min	Minute
mg	Milligramm
mL	Milliliter
MMD	Multi-Month Dispensing
mmol	Millimole
MTB	Mycobacterium Tuberculosis
MTCT	Mother-to-Child Transmission
MSM	Men Who Have Sex with Men
N	Number
NA	Narcotics Anonymous
NAFLD	Non-Alcoholic Fatty Liver Disease
NCCPP	National Cervical Cancer Prevention Programme
NCDs	Non-Communicable Diseases

NFLD	Non-Fatty Liver Disease
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NTRL	National Tuberculosis Reference Laboratory
OD	Once Daily
OIs	Opportunistic Infections
OTB	Optimized Treatment Backbone
PAP Smear	Papanicolaou Test
PCP	Pneumocystis Jirovecil Pneumonia
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
PIs	Protease Inhibitors
PID	Pelvic Inflammatory Disease
PLHIV	People Living with HIV
PLWA	People Living With AIDS
PML	Progressive Multifocal Leukoencephalopathy
PMTCT	Prevention of Mother-to-Child Transmission
PO	By Mouth
POPs	Progestin-Only Oral Contraceptive Pills
PrEP	Pre-Exposure Prophylaxis
PTB	Pulmonary Tuberculosis
PTSD	Post-Traumatic Stress Disorder
PV	Pharmacovigilance
PVL	Priority Viral Load
q	Every
RFT	Renal Function Tests
RIF	Rifampicin
RPR	Treponema Pallidum
RT	Resistance Testing
SRH	Sexual Reproductive Health
SSRI	Serotonin Reuptake Inhibitors
STIs	Sexually Transmitted Infections
T2DM	Type 2 Diabetes Mellitus
TB	Mycobacterium Tuberculosis
TMP-SMX	Trimethoprim/Sulfamethoxazole
TPHA	Treponema Pallidum Hemagglutination
TPT	Tuberculosis Preventative Therapy
TST	Tuberculin Skin Test
Tx	Treatment
U=U	Undetectable = Untransmittable
UDS	Urethral Discharge Syndrome
ULN	Upper Limit of Normal
VDS	Vaginal Discharge Syndrome
VIA	Visual Inspection with Acetic Acid
VIR	Vascular Interventional Radiology
VL	Viral Load
VMMC	Voluntary Medical Male Circumcision
WCC	White Cell Count
Y/N	Yes / No

Abbreviations: Institutions

BBCCCOE	Botswana-Baylor Children's Clinical Centre of Excellence
BHP	Botswana Harvard AIDS Institute Partnership
BHHRL	Botswana Harvard HIV Reference Laboratory
BOCAIP	Botswana Christian AIDS Intervention Programme
BOFWA	Botswana Family Welfare Association
BoMRA	Botswana Medical Regulatory Authority
BONELA	Botswana Network on Ethics, Law and HIV/AIDS

BOSASNET	Botswana Substance Abuse Support Network
BNTP	Botswana National Tuberculosis Programme
BSRHI	Botswana Sexual and Reproductive Health Initiative
CDC	Center for Disease Control and Prevention
DAIDS	Division of AIDS (US National Institutes of Health)
DHAPC	Department of HIV/AIDS Prevention & Care
EACS	European AIDS Clinical Society
NCCP	National Cancer Control Programme
NHL	National Health Laboratory
MoH	Botswana Ministry of Health
UNAIDS	Joint United Nations Program on HIV/AIDS
WHO	World Health Organization

Abbreviations: Antiretrovirals

3TC	Lamivudine
ABC	Abacavir
pALP	Pediatric FDC- ABC/3TC/DTG
ATV	Atazanavir
ATV/r	Atazanavir/Ritonavir
AZT	Zidovudine
CAB LA	Long Acting Injectible Cabotegravir
CBV	Combivir
DOR	Doravirine
DTG	Dolutegravir
pDTG	Pediatric Dolutegravir
DRV	Darunavir
DRV/r	Darunavir/Ritonavir
EFV	Efavirenz
FTC	Emtricitabine
INSTI	Integrase Inhibitor
LPV/r	Lopinavir/Ritonavir
NVP	Nevirapine
RAL	Raltegravir
RIT	Ritonavir
RPV	Rilpivirine
TAF	Tenofovir Alafenamide
TDF	Tenofovir
TLD	Tenofovir disoproxil/3TC/Dolutegravir
TRU	Truvada
XTC	3TC/Lamivudine/Emtricitabine
ZVD	Zidovudine

CHAPTER 1
HIV Combination Prevention

Always educate clients to understand that using an integrated approach to HIV prevention is best to prevent HIV transmission. These include:

- Annually HIV Testing (or more often as appropriate)
- Initiating ART immediately after an HIV positive diagnosis
- Offering voluntary medical male circumcision
- Promptly seeking treatment for Sexually Transmitted Infections (STIs) as soon as pain, dysuria, urethral discharge or vaginal discharge are detected.
- Always using condoms correctly and consistently
- Initiating Pre-Exposure Prophylaxis (PrEP) to protect those who engage in high-risk sexual activities (such as multiple concurrent partnerships, transactional sex, particularly Female Sex Workers (FSW) and Men who have Sex with Men (MSM)).

1.1 Methods of HIV Combination Prevention

1.1.1 Condom Use

Condom use is the safest option when couples are unsure of their sexual partners' HIV status or whether they are virally suppressed on ART. However, to avoid STIs and pregnancy the consistent and correct use of condoms is advised. Condoms should not be promoted as an effective contraception method but rather as a mean to ensure sexual reproductive health.

1.1.2 Undetectable = Untransmittable (U=U)

When an HIV sexual partner is virally suppressed (VL <200 copies/mL), there is much less risk of transmitting HIV to their sexual partners. Therefore, whether clients are in monogamous or non-monogamous HIV discordant sexual partnerships, the HIV positive partner should always maintain complete viral suppression (VL <200 copies/mL). Clinicians should advise accordingly based upon the individuals and couple's particular HIV, STI and pregnancy risks.

It is critically important to understand, that sexual encounters without the use of condoms can expose both HIV positive and negative individuals to contract serious STIs and become pregnant.

1.1.3 Post Exposure Prophylaxis (PEP)

Universal precautions must always be taken by healthcare providers (or anyone else exposed to infectious materials). If an exposure to infectious material or blood occurs, immediately (ideally within 1-4 hours) administer PEP as outlined in *Annex 1: Post-Exposure Prophylaxis (PEP).*

Individuals who experience a "condom burst" are also now eligible to receive PEP within 72 hours of exposure from healthcare facilities.

1.1.4. Male Circumcision

1.1.4a Infant Circumcision:

There are numerous advantages to early circumcision and all families should be encouraged to circumcise infants as soon as medically possible, ideally before the age of 2 months - preferably before 6 weeks. Note the following:

- Infant circumcision is simpler and safer than in older boys.
- No sutures are needed and there is quicker healing with less complications.

Contraindications include:

- Preterm babies ‹37 weeks' gestation
- Low birth weight (below 2.5 kgs)
    - Hematological Disorders
    - Jaundice or fever
    - Any congenital abnormality

1.1.4b Voluntary Medical Male Circumcision (VMMC)

Male circumcision substantially reduces the risk of female to male HIV transmission. The Ministry of Health has therefore embarked on targeted National campaigns to scale up access to circumcision to all eligible men, with the main focus on young men aged 15-29 years. Clinicians should make every effort to refer all males to local circumcision services.

It is important to educate clients that circumcision:

- Reduces HIV & STI transmission.
- Reduces risk of Penile and Cervical Cancer
- Does not eliminate the risk of HIV transmission.

Educate males regarding post circumcision care as follows:

- All sexually active males should engage in safer sexual practices such as correct and consistent condom use regardless of circumcision status.
- Caution that engaging in sexual activity while the circumcision (surgical) scar is not completely healed, will put them at risk for both acquiring HIV infection and subsequently transmitting it to sexual partners.
- Counsel all circumcised males NOT to resume sexual activities until an experienced clinician (when possible, the practitioner who performed the procedure) has advised that it is safe.

Advise women to strongly encourage their male sexual partners and their sons to be circumcised as soon as possible.

1.1.4c VMMC Minimum Package of Care:

- Pre-operative provider-initiated HIV testing and counseling.
- Exclusion of symptomatic STIs and syndromic treatment if detected.
- Provision of condoms and promotion of correct and consistent condom use.
- Post-operative wound care and abstinence instructions.
- Age-appropriate counseling on risk reduction.
- Active linkage to other HIV prevention, treatment, care and support services.

HIV positivity does not exclude eligibility for VMMC.

1.1.5 Gender Based Violence (GBV)

Routinely screen for and address GBV and intimate partner violence (IPV). If a client discloses abuse, or if a provider suspects that a client is experiencing any form of violence, deliver first-line support by using the CDC **LIVES approach**:

- **Listen:** Listen to the client closely, with empathy and without judgement.

- **Inquire about needs and concerns**: Assess and respond to the client's emotional, physical and psychosocial needs, and assist to find practical solutions.
- **Validate:** Show the client that you understand and believe them.

- **Enhance safety:** Discuss a plan to protect the client from further harm.
- **Support the client** by helping them connect to clinical and/or non-clinical violence response services through referrals to community interventions such as: *Gaborone Women's Shelter (267-3900516), Childline (267-3900900), Bosasnet (267-3959119), BONELA (267-3932516), BOFWA (267-3900489), BOCAIP (267-3916454), Local Police Station 999.*

1.2 HIV Screening & Testing

HIV testing should be integrated across a variety of health services such as: TB, STI, Child Welfare Clinics, in addition to all inpatients (whose current HIV status is not documented within their medical records). Botswana has adopted the WHO differentiated HIV testing service delivery approaches to provide a variety of options for testing across diverse settings. These include self-testing, facility-based testing, community testing and index partner testing. All approaches must ensure the protection of patient confidentiality and empower communities, by decreasing stigma and social harm. Innovations of social network-based testing will also improve access and convenience of all HIV testing services.

Regardless of the approach, individuals must be informed that:

- PLHIV who have already confirmed their HIV status and initiated ART, should NOT undergo additional HIV testing *(this includes self-testing)*.
- During pre-test counseling, clients must be sensitized to the possibility of seeing "faint lines" on testing results. Rapid HIV test results that display "faint lines" should be considered as positive.

As Botswana remains a HIV- high-burden country annual HIV testing among those who are sexually active is still recommended. Clients who are identified as high-risk populations or who engage in high-risk sexual behaviors should test more frequently (every 3-6 months).

Consider increased frequency of HIV testing in the High Risk and Key Populations list below.

1.2.1 High Risk & Key Populations:

- Men Who Have Sex with Men.
- Female & Male Sex Workers.
- Individuals who engage in sex with more than one sexual partner (multiple concurrent partnerships).
- Individuals who do NOT use condoms.
- Women or Men who cannot negotiate safe sex with their partners.
- Individuals who exchange sex for money or assistance.
- Clients who admit to ongoing domestic or intimate partner violence.
- Uncircumcised sexually active males.
- Discordant couples with HIV positive sexual partners who are NOT virally suppressed to <200 copies/mL and who do NOT use condoms.
- Young Women and Men who engage in high-risk sexual behaviors of any kind.
- IV Drug Users and/or Recreational Drug Users and their HIV negative partners.
- Sero-discordant couples attempting to conceive.
- Individuals who require repeated treatment for STIs or the recurrent use of Post-Exposure Prophylaxis (PEP).
- Pregnant and breastfeeding women *(see Section 1.2.6)*.

1.2.2. Types of High-Risk Sexual Behaviors:

- Unprotected anal intercourse (receptive and insertive)
- Unprotected penile/vaginal intercourse

- Oral intercourse
- Sharing needles for recreational drug use
- Early sexual activity (before the age of 18 years)
- Sexual activities with active STIs or with partners who have active STIs
- Sexual violence (intended or otherwise)

While the expansion of HIV testing services remains a national priority, mandatory or coercive HIV testing is never acceptable. Always ensure that clients fully understand their HIV testing options and willingly give consent to be tested.

1.2.3 HIV Self-Testing (HIVST)

WHO promotes HIV self-testing as a convenient and confidential option that is safe, accurate and normalizes routine testing. Expanding provision of HIV self-testing improves and expands options for those who are reluctant to come forward, and/or engage in high-risk sexual behaviors and must test more frequently. HIV self-testing kits are now available in public health facilities and private pharmacies for purchase.

It is important to note, however that self-testing does not provide a definitive diagnosis for HIV positivity but should only be used as a triage for HIV diagnosis and as a link to HIV prevention services for those who test negative.

Remember:

- If the first HIV self-test is non-reactive, assume the client is HIV negative.
- If clients are unsure how to interpret their self-testing results, they should find a trained HIV testing provider or healthcare facility.
- As a rule, parents should not perform self-testing on their babies or children. However, assisted HIVST (i.e., guided by healthcare workers) may be useful for children and adolescents to provide a patient-centered approach and improve HIVST access.
- Remember, self-testing cannot detect HIV in children younger than 18 months of age.

Testing Definitions:

- T0 HIV Screening Test
- T1 The First HIV Confirmatory Test
- T2 The Second HIV Confirmatory Test

Follow the Algorithm for HIV Self-Testing, below:

Table 1: Algorithm for HIV Self-Testing (Using Determine/Unigold or 4th Generation HIV Test Kits)

HIV Self-Testing Algorithm	
Perform HIV Self-Test (T0)*	
If T0 is **Reactive**	Immediately link to further HIV Testing Services
If T0 is **Non-Reactive** (Negative result)	○ Link to HIV prevention services ○ Re-test after 3 months for accuracy during the "window period" ** ○ Re-test with any other HIV exposure or ongoing risk

*Self-Testing kits can be available as blood or saliva tests
**The "window period" of an HIV test is the time period between the exposure to HIV and the accurate detection of HIV infection through testing. Typically, this time period is 3 months.

To eliminate the possibility of an HIV negative person being placed on ART, all HIV positive rapid test results must undergo verification at all ART initiation sites before beginning treatment.

1.2.4 HIV Testing at Facilities & Confirmation of HIV Self-Testing Results

When using Determine or Unigold HIV Tests as the first rapid test (T1) confirmatory test – follow the algorithm that appears in *Annex 2: Testing Algorithm for Confirmatory HIV Testing using Determine & Unigold Testing Kits.*

Table 2: HIV Diagnosis Testing Algorithm: Using 4th Generation Test Kits

HIV Testing Algorithm ≥18 months of age
Perform testing with the first rapid HIV test (T1) (4th Generation HIV Test) for HIV screening ↓
If T1 (4th Generation) is negative, the client is diagnosed as HIV negative, Recommend annual HIV testing and refer the client to the appropriate HIV prevention services.
↓ If T1 is positive, repeat with a second rapid HIV test (T2-Unigold/Determine)
If T2 (Unigold/Determine) is positive, repeat with a third rapid HIV test (T3)
↓ **If T1 & T2 are all positive** The client is diagnosed as HIV positive and immediately refer and track the client to an ART initiation site.
If T1 (Determine) is Positive but T2 (Unigold) is Negative ↓ Repeat both T1 (Determine) & T2 (Unigold)
If the tests remain discordant Report both of these results as inconclusive. Send for PCR immediately and ask the patient to return in 7 days for the result.
Notify the National Reference Lab (BHHRL-Gaborone: 3902671 FT: 2441917) & The National HIV Testing Programme (3632313)
NOTE: The implementation of 4th Generation HIV Testing will begin in 2023 and these algorithms may be revised, as required.

1.2.5 HIV Testing for Infants & Children

Table 3: Algorithm for HIV Testing Children < 18 months

Revised HIV Testing Algorithm for Children <18 months of age
All low-risk HIV-exposed babies (not tested at birth) must complete DNA PCR testing at **6-8 wks** of age All High-Risk HIV-exposed babies should complete HIV-Testing at birth. (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.
HIV exposed babies identified as HIV negative at birth or at 6-8 weeks, whether they are breastfed or not, must retest again at **ALL** of the following time points: ▪ 6-8 weeks ▪ 3 months after cessation of breastfeeding ▪ 9 months of age ▪ 18 months of age *(by rapid test)* HIV testing should also be repeated when an infant/child: ▪ Appears sick, is growing poorly or has any developmental delays.
Remember: ▪ **If <18 months use DNA PCR** ▪ **If >18 months use rapid tests as outlined above.** **If DNA test results have not returned within 7 days – call the local laboratory that received PCR specimen to track the results.**

1.2.5a HIV Testing for Hospitalized Children

All children admitted into the hospital regardless of the status of the mother (including those found abandoned) should be considered as high-risk for HIV infection. If they do not have a documented HIV status (within the past year), test for HIV according to the age specific instructions outlined in Table 3 above.

1.2.5b HIV Screening at Child Welfare Clinics (CWC)

HIV-exposed babies must be clinically evaluated monthly at the child welfare clinic to detect the development of O.I.s or other HIV related illness. All health facilities must include HIV testing into their CWC algorithms.

- Discuss any HIV-exposed babies with WHO clinical stage 2, 3, or 4 conditions with a pediatric HIV Specialist for consideration for immediate ART initiation *(refer to Annex 3: HIV Specialist Directory)*
- DOCUMENT all babies' HIV results. If there are no documented results, immediately proceed with HIV testing.
- There should be a low threshold to re-test HIGH-RISK INFANTS that received triple ART prophylaxis and who do not have documented negative PCR results, if there are any clinical concerns.
- To ensure linkage, record mother's and/or relative's cell number and National Identification Number on all medical records and requisition sheets for children.

1.2.5c HIV Testing for Adolescents

Less than 16 Years of Age: An adolescent under the age of 16 years must obtain consent to be tested for HIV from a parent or legal guardian. However, when a qualified healthcare provider has determined that the adolescent is capable of understanding the consequences of their behavior and it is deemed in the best interest of the adolescent, parental or legal guardianship consent can be waived.

Emancipated Adolescents (Head of Households): An emancipated minor is one who is no longer under the care, custody, and control of his/her parents irrespective of their age. In Botswana, those below 16 years of age, who are pregnant, married or operating their own business, can be considered emancipated minors, DO NOT require the consent of their parents to be tested for HIV.

Furthermore, their parents do not have to be present during HIV counselling.

However, adolescents may choose to have a parent or another adult with them to provide the necessary support. This option should be discussed with the adolescent. It is also important to encourage family members who are assisting with the care of babies born to minors to be actively involved.

16 Years old and above: Adolescents aged 16 years or above are authorized to give full informed consent for HIV testing.

1.2.5d HIV Testing in Cases of Violence, Domestic Abuse or Rape *(regardless of age)*

- Across all HIV testing facilities, clients should be routinely screened for gender-based or intimate partner violence.
- Provide immediate HIV testing, comprehensive medical and psychological care as a matter of urgency whenever sexual abuse is identified.
- Abused children must have access to HIV testing.
- Those sexually abused must also access post-exposure prophylaxis (PEP) immediately after the incident, no later than 72 hours.

1.2.5e HIV Testing during Pregnancy & Breastfeeding

All HIV negative pregnant women (including non-nationals) must undergo HIV testing using the Triple point-of-care test for HIV, Syphilis & Hepatitis B. If the Triple Test is not available, these tests should be sent separately at the first Antenatal Clinic (ANC) encounter.

If pregnant women are found to be HIV positive.
Follow the algorithms for confirmatory HIV testing as listed above.

If breastfeeding, repeat HIV testing every three months and at three months after the cessation of the breastfeeding period, **regardless of how long breastfeeding takes place.**

HIV testing must be repeated at:

- Every trimester of pregnancy
- At delivery, if there is no HIV test result documented within the past 4 weeks.
- Between 6-8 weeks post-delivery

Follow the algorithm listed in Table 4, below.

Table 4: Algorithm for HIV, Syphilis & Hepatitis B Testing in Pregnancy & Breastfeeding

Testing During Pregnancy				
Registration and/or 1st Trimester	2nd Trimester	3rd Trimester	At Delivery	Post Delivery
HIV, Syphilis & Hepatitis Testing between 0-12 wks	HIV Testing between 13-28 wks	HIV & Syphilis Testing after >28 weeks but before delivery	If no HIV, Hepatitis and Syphilis test result are documented within the past 4 weeks	HIV Test between 6-8 weeks of after delivery
HIV Testing During Breastfeeding				
3 months Postpartum	6 months Postpartum	9 months Postpartum	All breastfeeding mothers must undergo HIV testing 3 months after cessation of the breastfeeding period.	

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 and postpartum.

Advise all HIV negative pregnant women that repeat HIV testing must be done whenever they have a possible exposure to HIV or STIs during pregnancy.

1.3 Pre-Exposure Prophylaxis (PrEP)

PrEP is the use of antiretrovirals by HIV negative individuals to prevent the acquisition of HIV. Initiation of PrEP requires that healthcare providers become competent and comfortable addressing

1.3.1. PrEP Eligibility & Contraindications

An individualized risk-benefit assessment must be conducted to determine PrEP eligibility.

- **All inquiries about PrEP should be taken seriously, as requesting PrEP has been shown to be indicative of participation in high-risk sexual behaviors.**
- **Healthcare providers should not discourage or frighten anyone about PrEP use, but rather be sensitive, inclusive, non-judgmental and supportive.**

Eligibility:

- 18 years of age, emancipated minors *and under certain circumstances other minors (see Section: 1.2.4, on eligibility for HIV testing in Adolescents <16 years of age)*
- Documented as HIV negative at PrEP initiation.
- **4th Generation HIV Testing must always be used when available.**
- At substantial risk of HIV infection.
- Normal renal function (i.e., Creatinine Clearance (CrCl) >60cc/min). Note: PrEP may be initiated while awaiting baseline results only in healthy clinically stable patients without co-morbidities.
- Willingness to use PrEP as prescribed including quarterly HIV testing.
- Pregnant and breastfeeding women.

Contraindications:

DO NOT prescribe PrEP in the following circumstances:

- HIV positivity
- CrCl/eGFR <60cc/min.

- Signs or symptoms of acute HIV infection are present (i.e., flu-like symptoms, fever, headache, rash, ulcers, myalgias, swollen lymph nodes, fatigue, etc…).
- Reported recent exposure to HIV - within the past 12 weeks. However, if 4th generation HIV testing is available this duration can be reduced to 4 weeks.
- Known allergy or contraindication to any medicine in the PrEP regimen.

1.3.2. PrEP for HIV Discordant Couples:

Inform discordant couples that when the HIV positive partner is virally suppressed (VL <200 copies/mL), it is extremely rare – if not impossible – to transmit HIV. **Therefore, complete viral load suppression is the best protection against HIV infection of the HIV negative partner.**

Remember U=U Undetectable = Untransmittable

However, if discordant couples prefer the added benefit of using PrEP, or if the discordant couple decide to become pregnant and request PrEP - it should always be provided.

PLHIV and HIV discordant couples should carefully consider their sexual and reproductive health and fully enjoy their sexual lives. Health care providers should encourage all their clients, including adolescents, to speak openly about their sexual choices.

1.3.3 PrEP during Pregnancy & Breastfeeding

Oral PrEP can be safely administered during pregnancy and breastfeeding. Follow the same general principles for PrEP counseling and initiation as outlined above.

- Pregnant women taking either form of PrEP must undergo HIV testing at 3-month intervals.
- Continuation of PrEP after pregnancy and breastfeeding should be encouraged for all women who engage in high-risk sexual behaviors *(see Section 1.2)*.

Note: Clinical trials on the safety of long-acting injectable PrEP in pregnancy and breastfeeding are underway with results expected beginning in 2024. Once implemented, long-acting CAB-LA would be preferrable to oral PrEP in pregnancy. Details of implementation will be communicated to all health facilities.

1.3.4 Counseling for PrEP

Counsel, educate and ensure that clients have a comprehensive understanding of the requirements for effective PrEP as one component of HIV combination prevention services (including condoms, lubricants, contraception, VMMC and STI management). **Always emphasize that strict adherence to all PrEP formulations is required for it to be effective.** This is particularly important for those who engage in condomless sex.

Counseling sessions must inform clients of the following:

- Using PrEP without condoms and contraception will not prevent infections from other STIs or pregnancy.
- It takes approximately 7 days of daily oral doses of PrEP to reach a protective concentration in the blood and other tissues. During this time, recommend the use of other preventive measures.
- Although the risk of HIV acquisition and the need for PrEP may change over time, discourage clients from starting and stopping PrEP indiscriminately without first discussing this with their healthcare providers.
- Inform clients to continue to take PrEP for 7 days after their last possible exposure to HIV, if discontinuing.
- PrEP users must undergo HIV clinical screening and testing every 3 months.

- Caution clients to seek prompt clinical care if they should develop any signs/symptoms of Acute HIV Infection.

Always Screen for Gender Based Violence and the possible impact of intimate partner violence on PrEP adherence. Help the client to strategize ways to safely take PrEP with or without their partner's knowledge. **The disclosure or suspicion of GBV points to the importance of initiating PrEP and does not disqualify a client from PrEP eligibility.**

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

1.4 PrEP Initiation & Clinical Management

Safe clinical management of PrEP requires initiation by trained health care providers who can recognize signs and symptoms of acute HIV infection and other STIs. Once clients have tested for HIV and are found to be HIV NEGATIVE, provide adequate HIV clinical screening, initiate and continue PrEP, *as outlined in Table 5 below.*

Delayed initiation of PrEP has been associated with significant loss-to-follow-up (LU) and **Same-Day initiation of PrEP has been shown to be safe. When clients are clinically stable, showing no evidence of acute HIV infection, OIs or other clinical issues - Initiate Same-Day PrEP – even without baseline laboratory results.**

- **However, baseline labs must be drawn and results reviewed and tracked within 2 weeks of PrEP initiation.**
- **Follow the monitoring recommendations below:**

Table 5: PrEP Clinical Management and Initiation

Baseline visit	1 Month post- PrEP initiation, 3 months and every 6 months, thereafter	If found to be HIV Positive while on PrEP
Clinical Assessment Screen for acute HIV infection: Flu-like symptoms, fever, headache, myalgias, arthralgias & lymphadenopathy Complete: - HIV Testing (with 4th Gen Testing kits) - Hep B/HIV/Syphilis Testing - STI screening - Pregnancy Testing - Counseling & Education - Creatinine Clearance	- HIV testing - CrCl/eGFR - Pregnancy Testing - Adherence Assessment - Clinical Assessment - STI Screening - PrEP Counseling & Education - Management of side effects	- Stop PrEP immediately. - Provide pre-ART counselling. - Collect blood for ART baseline investigations, including HIV drug resistance testing. - Initiate ART immediately then follow-up resistance testing and other baseline results, within 2 weeks.
Before prescribing PrEP - it is the healthcare provider's responsibility to have the clinical capacity and mechanisms in place to adequately monitor and track all patients initiated on PrEP for the duration of its use. Should routine monitoring lab results not be available - in clinically stable clients - continue PrEP and send monitoring labs at their next 3 month follow up visit.		

PrEP Initiation for Men & Women
Initiate PrEP with TDF 300mg/FTC 200 OD *(as a fixed dose combination)* *Alternative Regimens:* ▪ **When available: Long-Acting Injectable Cabotegravir*** (administered once every 2 months) ▪ **For Men Only: TAF 25mg/FTC 200mg* OD** (when available can be used as an alternative option in cases of renal insufficiency or nephrotoxicity)
When using TDF/XTC for PrEP **DO NOT start (or continue) PrEP if CrCL/eGFR is ‹60 ml/min.**

1.4.1 Cycling On & Off PrEP

The duration of PrEP use may vary from person to person. Starting and stopping PrEP depends on personal needs and perceived risk at different time points in a person's life (i.e., changes in relationships and lifestyle).

- Encourage clients to openly discuss their preferences for starting and stopping PrEP.
- Educate for the need to continue PrEP for 7 days after the last HIV exposure before discontinuing (except for those practicing Event Driven PrEP).

1.4.2 Stopping PrEP

When there is no longer a substantial risk of acquiring HIV infection consider stopping PrEP. Discuss other available HIV prevention risk reduction strategies and explore the risks and benefits of each prevention measure.

Advise as follows:
- PrEP must be continued for 7 days after the last exposure to HIV infection.
- HIV testing will be required before re-initiating PrEP in the future.

PrEP must be stopped when:
- PrEP users test HIV positive.
- CrCl/eGFR drops below ‹60 mL/min.
- The risks of using PrEP outweigh the potential benefits.

1.4.3 Managing Seroconversion on PrEP

HIV seroconversion while taking oral PrEP can occur without strict adherence or if HIV infection was undiagnosed at the time of PrEP initiation. Immediate transition from PrEP to HIV treatment will decrease acute viral load, immunological injury and secondary HIV transmissions.

If someone taking PrEP tests positive for HIV (seroconverts):

- Immediately stop PrEP and initiate first line antiretroviral therapy without delay.
- Send an HIV resistance test on the same day as ART initiation. However, **DO NOT withhold ART while awaiting resistant testing or other laboratory results.**

1.4.4 Special Considerations with PrEP

- **Hormonal contraception:** There is no known drug interactions between TDF/FTC and oral, injectable or implanted hormonal contraceptives.
- **Hepatitis**: As TDF, 3TC and TAF are active against Hepatitis B infection, always continue their use in clients who are Hepatitis-B Surface-Antigen positive (HBVsAg+), even after they are no longer using PrEP.

1.5 Alternative PrEP Formulations:

1.5.1 Long-Acting Injectable Cabotegravir

The use of long Acting Injectable Cabotegravir (CAB LA) administered once every 2 months is currently the most effective method to prevent HIV infection (as proven in clinical trial HPTN 084, in which Botswana took part). CAB-LA has the potential to increase choice and overcome some of the barriers related to poor adherence from long-term use of oral PrEP.

The HIV Guidelines Committee therefore has endorsed the implementation of CAB-LA as PrEP, pending affordability.

1.5.2 Event-Driven 2-1-1 PrEP (ED-PrEP) or "PrEP on Demand" for Receptive Anal Sex for MSM

Intermittent use of PrEP (Event- Driven PrEP) is a safe alternative for MSM who are not subject to ongoing risk but who could benefit from taking PrEP only when at risk *(see Table 6 below)*. However, this should not be an option for men (or women) that are at on-going risk who should be strongly advised to use continuous PrEP.

Table 6: Event Driven PrEP for MSM

Event-Driven PrEP (ED-PEP or PrEP on Demand) 2-1-1 Only for Intermittent Receptive Anal Sex for MSM		
Loading Dose taken 2 to 24 hours **before** sex	**24 Hours after** the first loading dose	**24 Hours after** the second dose
2 Tablets of TDF/XTC or TAF/FTC	1 tablet TDF/XTC or TAF/FTC	1 tablet TDF/XTC or TAF/FTC
Clients who might engage in repeated anal sexual acts past 24 hours should remain on PrEP for as long as their sexual activates continue, stopping only after 7 days of their last sexual encounter. It is important that young women are counselled to understand that engaging in anal sex to protect their virginity constitutes a high-risk sexual behavior and Event-Driven-PrEP is NOT effective to protect them from HIV acquisition.		

CHAPTER 2
Pregnancy Planning & Prevention for Women Living with HIV

2.1 Planning Pregnancies

If your patient would like to become pregnant, be supportive of this decision and give comprehensive safer conception and pregnancy planning advice.

2.1.1. Discordant & Seropositive Concordant Couples who wish to have Children

Providers should encourage PLHIV and their partners to speak openly about their reproductive plans and desires and assist them to make well informed decisions regarding pregnancy.

- Remember, Undetectable = Untransmissible (U = U) *(see: Section 1.1.2).*
- Always support good adherence and counsel PLHIV to wait until their viral load is fully suppressed (VL <200 copies/mL) before trying to conceive.
- If one or both partners has a detectable viral load, discuss the risks of unprotected sex (i.e., the risks of HIV transmission, HIV superinfection and STIs).
- Provide thorough counseling on safer conception options, including the use of PrEP for the HIV-negative partner to prevent HIV transmission while trying to conceive.
- All women planning a pregnancy – whether or not they are living with HIV – should be advised to take a folic acid supplement (5mg OD) daily while trying to conceive and for the first 12 weeks of pregnancy, to reduce the risk of fetal neural tube defects.
- Ideally, women should be clinically stable and their pregnancies should not compromise their health.
- To avoid complications, it is best for women planning pregnancies to have CD4 counts above 200 cells/mL, without evidence of opportunistic infections.

Mothers who test positive for HIV during pregnancy or at delivery should immediately be initiated on ART.

2.2 Pregnancy Prevention:

Women living with HIV and their partners have a fundamental human right to a satisfying and safe sexual and reproductive life. Preventing unintended pregnancies and safely planning desired pregnancies leads to improvements in maternal and child health and prevents mother-to-child transmission (MTCT). If women and their partners choose pregnancy prevention, they should be offered comprehensive counseling as outlined below:

- Assist PLHIV with decision making about their family planning and pregnancy prevention in non-judgmental and sensitive ways.
- Inform women and their partners about the full range of contraceptive methods to help them to select the best method in terms of safety, effectiveness, and acceptability.
- Explain that no contraceptive method is specifically contraindicated because of HIV or while using ART and encourage them to choose the best method for their lifestyle from the range of methods available, if the method is safe to use with their other medical conditions *(refer to section 1.2: WHO MEC, below).*
- Provide their contraceptive method of choice immediately or as quickly as is possible without delay.

2.2.1 Dual Protection with Condom Use

Dual protection is the consistent use of a male or female condom (a 'barrier method') along with another effective method of contraception. Always recommend "dual method" use for the most effective prevention of both HIV and STI transmission as well as pregnancy prevention.

Remember:

- HIV infection and/or HIV medication are not barriers to any method of contraception.
- No method of contraception increases risk of HIV acquisition.
- No method of contraception impairs the effectiveness of ART.
- Always advise the use of dual protection: The use of a condom alongside another effective method of contraception to offer best protection against STIs/HIV and unintended pregnancy.
- Undetectable = Untransmissible ('U = U'), meaning women and their partners who know their HIV status and are virally suppressed on ART can be supported to conceive safely.

2.2.2 Contraceptive Methods Available in Botswana

Each of these contraceptive methods are described in more detail in Annex 4: Key Points for Common Methods of Contraception in Botswana, including HIV Considerations.

Non-hormonal methods:

- Copper-bearing intrauterine device (Cu or copper IUD, called the "loop" or "coil", which lasts 5 to 12 years depending on the specific type).
- Male and female condom
- Female (tubal ligation) and male (vasectomy) sterilization (permanent methods).

Hormonal methods:

- Hormone-releasing IUD (progestin-only, called the LNG IUD or Mirena®, lasts 5 years) only available in the private sector.
- Progestin-only subdermal contraceptive implants (Implanon NXT® is one rod containing etongestrel lasting 3 years; Jadelle® is two rods containing levonorgestrel lasting 5 years).
- Progestin-only 3-monthly injectable contraceptive containing depo medroxy progresterone acetate (known as Depo-Provera®, Petogen® or DMPA, referred to here as DMPA).
- Combined oral contraceptive pills (COCs) (estrogen plus progestin).
- Progestin-only oral contraceptive pills (POPs).
- Contraceptive vaginal ring (combined estrogen plus progestin), only available in the private sector.
- Contraceptive patch (combined estrogen plus progestin), currently available in the private sector.

When counselling patients about the different contraceptive methods, consider using a 'tiered approach', starting first with the most effective methods *(see Table 7 below)* but covering all options.

Table 7. General Effectiveness of Contraceptive Methods with "typical" use

Level of effectiveness		Method and unintended pregnancy rate			
Most effective ↑ Least effective	Less than 1 pregnancy per 100 women in a year	**Implant** 0.05%*	**Intrauterine device** LNG IUD-0.2% Cu IUD-0.8%	**Male sterilization** 0.15%	**Female sterilization** 0.5%
	6-12 pregnancies per 100 women in a year	**Injectable** 6%	**Pill** 9%	**Patch** 9%	**Ring** 9%
	18 or more pregnancies per 100 women in a year		**Female condom** 21%	**Withdrawal** 22%	
		Fertility awareness methods 24% *(i.e., calendar or symptom-based methods)*	**Male condom** 18%		
		* The percentages indicate the number out of every 100 women who experienced an unintended pregnancy within the first year of typical use (how methods are commonly used) of each contraceptive method.			

2.3 The World Health Organization (WHO) Medical Eligibility Criteria (MEC) for Contraceptive Use

Helping a patient to determine the best contraceptive method for them should be informed by the woman's preferences and the WHO MEC guidance on contraceptive method safety, as described below.

Use the WHO MEC to determine whether a patient is medically eligible and can safely use a particular contraceptive method **in the context of her various health conditions, characteristics and any special circumstances**, including high HIV risk and HIV infection.

- For example: A patient may present living with HIV on ART but also have hypertension, obesity, and be recently postpartum. Each of these health conditions and characteristics need to be considered in contraceptive counselling and provision.

Recent updates to the guidelines (World Health Organization Medical Eligibility Criteria for Contraceptive Use, 5th Edition (2015) are available on the WHO MEC Contraception Tool 'App', available to download for free to your smartphone: search for 'WHO contraception tool' in Google Play or the App Store. There is also a Botswana MEC Wheel (updated 2017) which should be available for reference in most clinics.

In the MEC classification system, there are 4 categories *(see Table 8 below).*

- Check the MEC category for **each of a patient's reported medical conditions**, characteristics and/or special circumstances.
- MEC Category 1 or 2 indicates that it is always or generally safe to use the method with respect to the particular health condition, characteristic and / or special circumstance.
- MEC Category 3 indicates a health condition where the theoretical or proven risks may outweigh the benefits, while MEC Category 4 indicates a health condition where there is an unacceptable health risk if the contraceptive method is used.
- It is important to note that ALL contraceptive methods are MEC Category 1 or 2 for HIV infection and HIV medications, which means that women living with HIV have many contraceptive options.

- In the case of MEC Category 3 or 4 methods, where alternative contraceptive methods are not available or acceptable to the patient, consult a SRH Specialist about suitable options *(see HIV Specialist List in Annex 3).*

Table 8: How to Use the WHO MEC

MEC category	MEC category description	Use of MEC categories in clinical practice	
		With clinical judgment	With limited clinical judgment
1	A condition for which there is NO restriction for the use of the contraceptive method	Use method in ANY circumstances	YES Use the method
2	A condition where the advantages for using the method generally outweigh the theoretical or proven risks	Generally, use the method; some follow-up may be needed	
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method	Use of the method not usually recommended unless other more appropriate methods are not available or not acceptable. Clinical judgment and continuing access to clinical services are required for use.	NO DO NOT use method
4	A condition which represents an unacceptable health risk if the contraceptive method is used	Method should not be used	

Table 9. Adapted Summary of MEC Categories for Selected Contraceptive methods and specific ART drugs according to the 5th WHO MEC for Contraceptive Use (2015).

	Combined Hormonal Contraception*	POP**	DMPA progestin-only injectable	Progestin-only implant	LNG IUD*** Initiation	LNG IUD*** Continuation
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)						
ABC, TDF, TAF, AZT, 3TC/FTC	1	1	1	1	2	2
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)						
Etravirine (ETR) and Rilpivirine (RPV), Doravirine (DOR)	1	1	1	1	2	2
Protease inhibitors (PIs)						
ATV/r, DRV/r, RTV	2	2	1	2	2	2
Integrase inhibitors						
Dolutegravir (DTG)	Hormonal contraception (i.e., implant, oral contraceptive, ring and patch) can be effectively and safely used with DTG. Research has shown that DTG does not inhibit or induce enzymes involved in steroid hormone metabolism.					

*CHC (combined hormonal contraception) includes the combined oral contraceptive pill, the contraceptive ring and the contraceptive patch. ** POP (progestin-only oral contraceptive pill). ***The LNG IUD (levonorgestrel-releasing intrauterine system, aka Mirena®) is currently only available in the private sector in Botswana.

Key information points for providers: medical eligibility criteria and drug-drug interactions

- The copper IUD is a highly effective and safe method for women and adolescent girls living with HIV. It does not interact with any ART and/or TB medications.
- The DMPA injection also avoids interactions and is effective when used alongside all HIV and TB medications.
- With respect to hormonal contraception and HIV medication use, MEC Category 2 denotes a drug interaction potentially causing reduced efficacy of the contraceptive method, unless

otherwise stated. However, these MEC Category 2 methods can still be used with counseling and where other options are not suitable.

- It is recommended that providers use comprehensive and regularly updated drug interaction resources (see University of Liverpool HIV Drug Interaction Checker (https://hiv-druginteractions.org/checker). All of a patient's ART and other medications, including contraceptives, can be entered into this website to check for possible interactions.
- Where drug interactions exist or are possible, but other contraceptive methods are not available or acceptable to the client, you can still provide the method and emphasize the importance of correct and consistent condom use in addition to the contraceptive method ("dual method use") *(See Section 2.4: 'Drug-drug interactions, below).*
- Emergency contraception can be used by women and adolescent girls on HIV medications. Those taking enzyme-inducing ART (NNRTI & PIs) and/or TB medications may require a higher dose of emergency contraception pills. *(See Table 10 below for details).*

Help patients to avoid unintended pregnancies, regardless of their HIV infection status.

2.4 Drug-Drug Interactions with Contraception

Dolutegravir and hormonal contraception
The widespread roll-out of dolutegravir-based ART in Botswana allows a wider range of very effective contraceptive options for women living with HIV, particularly in the long-acting reversible contraception (LARC) category, as drug-drug interactions (DDI) between dolutegravir and hormonal methods of contraception, including the contraceptive implant, LNG IUD, DMPA injectable, combined hormonal contraception, progestin-only pills, and emergency contraceptive pills are not expected and none have been documented by research .

When considering DDI from other antiretroviral medications and hormonal contraception: The ART drugs most associated with ART-contraceptive DDIs are efavirenz (a component of TLE), ritonavir-boosted protease inhibitors and other ART medications not currently used in Botswana.

Contraception and ART interactions do not decrease the effectiveness of the HIV medications. However, these interactions can potentially lead to decreased effectiveness of some of the hormonal contraceptive methods. When potential for DDIs exist, counsel woman on the potential for drug interactions and risk of unintended pregnancy and document the counselling session.

- Some hormonal contraceptives (i.e., implant, oral contraceptives, ring and patch) are safe but may become less effective with some HIV & TB medications.
- Some hormonal methods (i.e., particularly implants) can still be effective and in some cases may even be the most effective method for a particular woman taking certain HIV medications - if other methods are inappropriate or unacceptable to her or she cannot adhere well to other methods.
- There is no evidence that DMPA injection increases the risk of an HIV-uninfected woman acquiring HIV. Therefore, there should be no restrictions on the use of DMPA for women living with HIV or women at high risk of HIV infection.

2.5 Emergency Contraception (EC)

Emergency contraception (both emergency contraceptive pills (ECPs) and the emergency Cu IUD can be safely used by women at risk of or living with HIV. Always offer emergency contraception if a woman presents to a healthcare service within 5 days of unprotected sex. Emergency contraception should additionally be offered in the case of contraceptive nonadherence or failure (e.g., 2 or more

missed COCPs, late or missed POP, more than 14 weeks since last DMPA injection or condom failure) where unprotected intercourse has occurred; or in the case of sexual assault.

In cases of sexual assault, PEP should always be offered *(see Annex 1)*. Oral EC is commonly known as "The Morning After Pill".

- **Insertion of the emergency Cu IUD** within 5 days (120 hours) of unprotected intercourse or within 5 days of earliest predicted ovulation is the most effective EC *(See Table 10 below, for details of how to safely initiate the Cu IUD as EC)*. It also provides effective ongoing contraception.
- If a woman chooses and is eligible for the Cu IUD as her method of emergency contraception but it is not possible to provide this at the time, she should also immediately be given oral EC while awaiting IUD insertion.

Oral emergency contraception (oral EC) can also be used up to 5 days from unprotected intercourse *(see Table 6 below for oral EC types and dosing regimens)*.

- However, oral EC has lower effectiveness than the Cu IUD, especially beyond the first 24 hours after unprotected sex.
- The effectiveness of oral EC is highly variable depending on type of oral EC and duration of time since unprotected sexual intercourse, and in relation to timing of ovulation.
- If vomiting occurs within 2 hours of taking an oral EC, the dose should be repeated.
- Oral EC can be used more than once in a menstrual cycle.
- Women living with HIV taking enzyme-inducing ART (NNRTI or PIs) or TB medications may require an increased dose of oral EC *(see Table 10 below)*.

The Cu IUD should be considered first-line **emergency contraception for women taking enzyme-inducing ART or TB medications (if suitable for and acceptable to the patient) who wish to avoid pregnancy. Discuss with an SRH Specialist as needed.**

Table 10: EC Pill Regimens and How to Initiate the Cu IUD as Emergency Contraception

EC pills	Regime for patients NOT using enzyme-inducing drugs*	Regime for patients using enzyme-inducing drugs*
Combined Oral Contraceptives for Emergency Contraception		
Nordette®/Oralcon® (30µg ethinyl estradiol + 150µg levonorgestrel) *Typically considered, "the Morning After pill"*	4 pills immediately followed by 4 pills 12 hours later	Copper IUD should be recommended first-line. (6 pills immediately followed by 6 pills 12 hours later)
Progestin-only pills for Emergency Contraception		
Levonorgestrel dedicated emergency contraception pills (1.5mg levonorgestrel)	1.5mg tablet as a single dose OR 750mcg tablet immediately followed by 750mcg tablet 12 hours later	Copper IUD should be recommended as first line. (double dose of Levonorgestrel recommended: 3mg)
Cu IUD for Emergency Contraception		

Antibiotic cover for emergency IUD insertion may be advisable in some cases: Antibiotic cover should be given if a woman is considered at high risk of an STI.

If Cu IUD is selected for EC, but not as ongoing contraception, it can be inserted and then removed during the next menstrual period.

Timing of Cu IUD insertion as emergency contraception:
A urine pregnancy test can be performed to **exclude an established pregnancy** before providing an emergency IUD. However, a urine pregnancy test **cannot** exclude an early luteal phase pregnancy (first 21 days of pregnancy) so the following guidance must be followed even in the case of a negative urine pregnancy test. Follow the timing guidance below:

- A Cu IUD can be inserted **within 5 days (120 hours)** of the **first** episode of unprotected sex since the last menstrual period. and/or **Up to 5 days after the earliest estimated date of ovulation in a regular cycle** (i.e., up to day 19 of a normal 28-day cycle)

When patients know their cycle length and it is regular, enabling accurate estimation of the time of ovulation, the Cu IUD can be inserted beyond 5 days after intercourse, if this is not more than 5 days after earliest predicted ovulation.

Note: Cu IUD used as emergency contraception is NOT an abortifacient and will NOT cause an abortion.

2.6 Safe Abortion and Post-Abortion Care

Abortion is legally permitted in Botswana up to 16 weeks' gestation under specific circumstances, including:

- Rape, defilement and incest
- If the woman's health is at risk
- In the event of significant fetal abnormalities

Abortion can only be performed by registered medical practitioners within a government hospital or an approved private hospital.

- Providers should support clients who meet the legal parameters for abortion to seek safe abortion services, by making referrals to the appropriate services, such as Obstetrics and Gynecology specialists.
- Patients presenting with complications of an abortion, either spontaneous or induced, should be assessed and managed promptly and appropriately at facility level. When required, refer to a medical center that offers comprehensive post-abortion care (CPAC) services.

2.7 Special Considerations for Women Living with HIV aged over 40 years

Natural decline in fertility occurs with age and spontaneous pregnancy is rare after the age of 50. Women over the age of 40 who are sexually active and want to avoid an unintended pregnancy should use effective contraception until they reach menopause.

- Although pregnancy and childbirth after 40 years confer a greater risk of adverse maternal and neonatal outcomes, support the reproductive choice of women at all ages.
- Age alone does not restrict contraceptive method choice, therefore consider the comorbidities and background health risks using the WHO MEC, as women in the perimenopause will have different characteristics and health risks.
- Support women over 40 who are interested in long-acting reversible or permanent methods of contraception.
- Always counsel women about dual method use for protection against STIs in addition to pregnancy prevention.

2.7.1 HIV, Perimenopause & Menopause

Menopause is a natural process that all women experience. Natural menopause is deemed to have occurred after 12 consecutive months without menstruation for which there is no other obvious physiological or pathological cause and in the absence of clinical intervention. Menopause can also be induced as a consequence of surgical procedures that involve removal of both ovaries or medical interventions that cause cessation of ovarian function (i.e., radiation or chemotherapy). Diagnosis can usually be made on a clinical basis, specific blood tests for menopause are not usually required.

It is important that clinicians document menstrual patterns and menopausal symptoms in all women living with HIV (usually between 45 and 56 years), including hot flushes, sweats, sleep disturbance, genitourinary symptoms and changes in mood. Some women living with HIV may experience menopausal symptoms more severely or at an earlier age.

Women should be provided with information regarding perimenopause and menopause including possible treatment options and advice on lifestyle modification aimed at reducing menopausal symptoms. Many types of hormone replacement therapy (HRT) can be provided
to women living with HIV, but it is important to consider potential for drug-drug interactions and other comorbidities that may increase risks of complications for venous thromboembolism.

- Exercise caution with the use of HRT for women on DAR/r and DOR containing regimens as results of clinical trials are underway. Consult an SRH specialist for further advice if required.
- Integrating healthier dietary & lifestyle choices (i.e., decreases in sugar intake, alcohol, tobacco cessation and regular exercise) have been found to decrease menopausal symptoms.

Monitor the development of osteopenia and osteoporosis during menopause and of women exposed to TDF containing regimens.

- Educate women on maintaining healthy bones with diet, exercise and at least 20 minutes of sunlight exposure daily.
- **In the private sector**, refer suspected cases of osteopenia/osteoporosis for DexaScan for management and appropriate treatment.

CHAPTER 3
Infant Testing, Prevention of Mother to Child Transmission & Feeding

3.1 Infant Testing Schedules:

- Send HIV DNA PCR (Dried blood spot or whole blood):
  - **Test infants at LOW-RISK for HIV transmission between 6-8 weeks of age**
  - If testing is missed, it ***can be done at any age*** between 6 weeks and 18 months.
  - **Test infants at HIGH-Risk for HIV transmission at birth**
  - Birth testing only identifies in utero infections. Therefore, if the birth PCR is negative, 6-8 weeks HIV testing should be done to identify peri-natal infections.
  - All High-Risk infants who test positive at birth must be immediately reported to the PMTCT Programme at the Ministry of Health.
  - **Clearly document the contact details for infants who test positive through birth testing for tracking purposes and longitudinal follow up.**
- **Re-test during the first 18 months of age** after a negative test if the child:
  - Appears sick, is growing poorly or is developmentally delayed.
- **Re-test 3 months after complete cessation of breastfeeding**
  - If Positive, immediately initiate ART and send a confirmatory DNA PCR.
  - Do not wait for the confirmatory PCR to return before ART initiation.
  - If Negative, re-test with a Rapid Test at age 18 months to confirm child is negative. (DNA PCR at 6 weeks is 98-99% sensitive).
- **Re-test at 9 months DNA PCR** (for all HIV exposed babies)
- **Re-test at 18 months Rapid HIV Test** (for all HIV exposed babies)

3.2. Neonatal ART Interventions

Low-Risk HIV Exposed Infants, those whose MOTHERS:

- Started ART at least 12 weeks prior to delivery.
- Have no evidence of poor adherence to ART in pregnancy.
- Have no evidence of detectable viral load in the third trimester.

Administer a 28-day course of AZT to the infant as soon as possible, **at least within 72 hours of delivery**, as follows:

- Begin AZT 4mg/kg PO every 12 hours for 4 weeks.
- Pre-term or low birth weight, give AZT BD *(refer to dosing chart)*

3.2.1 Management For High-Risk HIV Exposed Infants

Infants whose mothers' HIV status is unknown and present <72 hours of delivery should be considered High-Risk for HIV transmission and immediately initiated with triple ART and **NOT initiated on AZT prophylaxis**. Also, immediately test Mothers for HIV, Syphilis and Hepatitis.

High-Risk Infants are born to Mothers who:

- Started ART less than 12 weeks from delivery.
- Viral load is not suppressed (>200 copies/mL) during their third trimester or at delivery.

- Defaulted ART during their pregnancy
- Admits to poor adherence during their pregnancy.
- Seroconverted during pregnancy and have no documentation of achieving VS.

IMPORTANT NOTE: ***Mothers who have previously documented long-term viral load suppression - but at delivery have missing or currently unknown viral loads (within the last 6 months) should not indicate high risk status if no other risk factors are present.***

Begin three-drug ART prophylaxis for high-risk infants with AZT, 3TC, NVP*.

- At 6 weeks test all high-risk infants to determine their HIV status in order to decide whether to continue ART.

NOTE: **False negative testing can occur in the setting of 3-drug ART; any infant with signs or symptoms of HIV following infant PEP discontinuation should be immediately retested.**

- For infants testing positive, switch immediately to ABC/3TC/DTG when the baby weighs ›3Kg *(see Table 11 below).*
- *NVP will be substituted with DTG as the dosage and safety in neonates is established.
- Report all infants testing positive to the PMTCT programme at the Ministry of Health for long-term monitoring and confirmation of results.

Diligently monitor and report all adverse birth outcomes of HIV positive women regardless of their ART regimens.

Table 11: Neonatal ART Dosing Chart

ART	Age in Weeks	Gestational Age (Dose in *mg/kg*)		
AZT		‹30 weeks	›30‹35 weeks	›35 weeks
	Birth to age 4 weeks	2 mg/kg/dose BD	2 mg/kg/dose BD	4 mg/kg/dose BD
	4 weeks to 8/10 weeks	3 mg/kg/dose BD	3 mg/kg/dose BD	12 mg/kg/dose BD
	Aged ›8 to 10 weeks	12 mg/kg/dose BD	12 mg/kg/dose BD	12 mg/kg/dose BD
3TC	‹4 weeks	2 mg/kg/dose BD		
	›4 weeks	4 mg/kg/dose BD		
	Gestational Age	Dosing		
NVP	32-34 weeks	2 mg/kg/dose BD (age Birth to 2 weeks) 4 mg/kg/dose BD (age 2-4 weeks) 200 mg/m² of body surface area (BSA) per dose twice daily (Age ›6weeks		
	34-37 weeks	4 mg/kg BD for 1 week, then 6 mg/kg BD thereafter		
	›37 weeks	6 mg/kg/dose BD		

3.3 Infant Feeding for HIV Positive Mothers

Breast is Best – When it is Safe

HIV positive women who are suppressed on ART should be encouraged to exclusively breastfeed their children for 6 months. However, there are circumstances when HIV positive mothers are not able to breastfeed because of their medical condition or because their viral load is not fully suppressed (>200 copies/mL), or there are concerns regarding adherence. Likewise, there are situations when formula feeding is not safe for example, due to unclean water supply. Therefore, before recommending breastfeeding to HIV positive women consider all aspects of a mother's social and medical situation.

The risk of HIV transmission from breastfeeding in Botswana is highest for women who initiate ART later in pregnancy and for those who are not fully virally suppressed (>200 copies/mL). It therefore remains the right of every HIV positive mother to decide whether to breastfeed her child based upon her circumstances and her decisions should be respected. Infant formula will remain available within the public sector to any HIV positive women who choose not to breastfeed.

When breastfeeding is chosen, advise women to:

- Exclusively breastfeed for the first 6 months of life, transitioning to formula feeding at 6 months.
- Introduce complimentary feeding at 6 months and continue breastfeeding and/or formula feeding (as preferred) until 12 months of age.
- Women may choose to extend breastfeeding to 12 months if they prefer while maintaining on-going viral load suppression.

HIV negative mothers who are breastfeeding should undergo HIV testing every 3 months

Regardless of the time of presentation, infant feeding counseling should be provided to ALL pregnant women starting at ANC.

3.3.1 Contraindications to Breastfeeding

If ANY of following conditions are present, advise HIV positive pregnant women NOT to breastfeed:

- Not yet on ART
- On ART without a documented viral load <200 copies/mL within the last three months *(if viral load testing is not available, discuss the situation with an HIV specialist)*
- ART was taken for less than 4 -weeks prior to delivery.
- Diagnosed HIV positive at time of labor.
- Serious adherence concerns.
- Maternal seroconversion occurs during pregnancy and not yet initiated on ART.

Mothers who are not able to breastfeed for any of the above reasons, must be educated in hygienic preparation of suitable milk substitute, also in hygienic care of feeding utensils.

- Provide formula for those mothers who cannot afford to buy the correct milk substitute.
- Always educate mothers on the critical importance of accessing clean water (boiled or purchased) to prepare safe formula.
- Assess whether these infant feeding plans are feasible, given mother's particular circumstances.

CHAPTER 4
Initiation of ART in Pediatrics

4.1 HIV Pediatric Care

Ensure that children's complete ART history is well documented. Include history of opportunistic infections, co-morbidities and PMTCT regimens. Take special care of children at high risk (i.e., orphans and vulnerable children (OVC) such as children of FSW or those from dysfunctional families) who are often neglected and underserved. Case management and referrals to supporting agencies may be required and helpful.

Prior to the initiation of ART in pediatric and adolescent patients always address:

- 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 their HIV status?
- If the child can appropriately dose medications, what adult will be responsible for supervising the child?
- Assist parents with developing strategies to ensure strict adherence.
- Disclosure has been shown to improve outcomes amongst children and adolescents living with HIV.

All infants and children who are found to be HIV positive must be immediately initiated on ART.

HIV exposed infants who have a clinical WHO stage 3 or 4 condition (or severe stage 2) but who do not yet have PCR results available should also be immediately initiated.

Discuss questionable cases with an HIV specialist as needed.
Do not delay cotrimoxazole prophylaxis.

4.2 Pediatric ART Dosing

Beginning in 2024, a new dispersible fixed dose combination (FDC) of pABC/3TC/DTG, known as pALD will become available in Botswana. This FDC can be used in children weighing 6-24.9 kgs. Children weighing less than 6kg will continue to use separate formulations, as outlined in Tables 12a & 12b, below.

Table 12a: ART Regimens for Children over 4 weeks; using Fixed Dose Combinations

Weight Band	Number of Tablets Per Day pALD: ABC/3TC/DTG 60/30/5 mg
6 to 9.9 kg	3
10 to 13.9 kg	4
14 to 19.9 kg	5

20 to 24.9 kg	6

Table 12b: ART Regimens for Children over 4 Weeks using Separate Formulations

Weight Band	1st Line Preferred Regimen	Separate Pediatric Formulations	
3-5.9 kg	ABC/3TC + DTG	pABC/3TC Dispersible tablet 120/60 mg (1 tab) OD	pDTG 10 mg Dispersible 5mg (half tablet) OD
6-9.9 kg	ABC/3TC + DTG	pABC/3TC Dispersible tablet 120/60 mg (1 and half tab) OD	pDTG 10mg Dispersible 15mg (1 and half tablet) OD
10-13.9 kg	ABC/3TC + DTG	pABC/3TC Dispersible tablet 120/60 mg (2 tabs) OD	pDTG 10mg Dispersible 20mg (2 tablets) OD
14-19.9 kg	ABC/3TC + DTG	pABC/3TC Dispersible tablet 120/60 mg (2 and half tab) OD	pDTG 10mg Dispersible 25mg (2 and half tablet) OD
20-24.9 kg	ABC + 3TC + DTG	pABC/3TC Dispersible tablet 120/60 mg (3 tablets) OD	DTG tablet 50 mg (1 tab) OD
›25 kg	TAF-ED	TAF-ED tablets 1 tab OD	

4.3 Pediatric ART Initiation - Special Considerations

Pediatric dolutegravir dispersible tablets are more bioavailable than film coated non-dispersible tablets. Therefore, 30mg DTG given as 3 x 10mg **dispersible** tablets is equivalent to one 50mg strength film coated tablet. Therefore, **DO NOT administer 5 x 10 mg dispersible paediatric formulated tablets to adults to replace 50mg formulations**

Remember:

- Use fixed dose combinations whenever possible to improve adherence.
- Increase DTG dosage to BD in combination with rifampicin.
- In cases of epilepsy, use valproate, lamotrigine, levetiracetam and topiramate. to prevent under dosing of DTG.
- If carbamazepine must be used, increase DTG to BD dosing.

4.3.1 Cotrimoxazole For Infants and Children

- Administer at 6 weeks, refer to Table 13 for dosage.

Give CTX to all HIV-exposed infants until PCR results are returned, as follows:

- After 6 weeks and a negative test: **IF NOT** breastfeeding:
- IF breastfeeding: Continue CTX until the infant's HIV status is determined 3 months after breastfeeding cessation.
- HIV positive children 1 to 5 years: CTX indicated if CD4% ‹25%
- HIV positive children ›5 years: CTX indicated if CD4% ‹15% or absolute CD4 count is ‹200 cells /µL.

4.3.2 Other Pediatric Indications for CTX :

- Active WHO stage 2, 3, or 4 conditions
- Virological failure (>200 copies/ mL)
- HIV positive children who have not yet initiated on ART for any reason.

Table 13: WHO Simplified CTX Dosing for Pediatric Patients

Age & Weight	Recommended Daily Dose	Suspension (5ML syrup= 200mg/40mg	Child Tablet 100mg/40mg	Single Strength adult tablet 400mg/80mg	Double Strength adult tablet 800mg/160mg
6wks – 6 m <5 kg	100 mg Sulfamethoxazole 20mg Trimethoprim	2.5mL	1 tablet	¼ tablet	-
6m – 5 yrs 5-15 kg	200 mg Sulfamethoxazole 40mg Trimethoprim	5 mL	2 tablets	Half tablet	-
6 to 14 yrs	400 mg Sulfamethoxazole 80 mg Trimethoprim	10 mL	4 tablets	1 tablet	Half tablet
Post-pubertal adolescents & adults	800 mg Sulfamethoxazole 160mg Trimethoprim	-	-	2 tablets	1 tablet

Chapter 5
Initiation of ART in Adolescents & Adults

5.1 Adults and Adolescents

Ensure that the patient's complete medical history (and any previous exposure to ART) is well documented within the patient's medical record. It is important to remember that some patients that have defaulted may present as treatment naïve but are not.

Carefully check both the electronic and manual medical records to identify any previous history of ART at initiation.

5.1.1 Adolescent Special Considerations

All clinics should identify staff members with an interest in adolescent care, who can provide (as much as possible) continuity of care. Designated staff members should form a 'therapeutic alliance' with adolescents, to help them handle challenges to their wellbeing. Whenever possible, provide family-centered disclosure support for those children transitioning to adolescents and adult care.

Continuity-of-care providers should also address issues of sexuality and adherence with adolescents, including:

- High risk sexual behaviors *(see Section 1.2.2)*
- Safe sex practices
- Substance abuse or recreational drug use
- Barriers to adherence and community support.

Notwithstanding the importance of family support for the adolescent, under certain circumstances 'parental consent' is NOT necessary to receive HIV services including HIV testing, PrEP and SRH.

5.1.2 In Naïve, Returning Defaulters (>90 days) or Previously LTFU

- Confirm HIV positivity in all newly identified patients to initiate ART *(see Section 1.2.4)*
- Screen for Advanced HIV disease: TB, cryptococcal meningitis, OIs, COVID-19 as indicated. *(See Chapter 7)*
- Complete a comprehensive physical examination to identify all OIs and co-morbidities.
- Review or send baseline laboratories, including CD4 count.
- Educate and advise newly identified HIV patients that they remain infectious until their viral loads are fully suppressed (VL <200 copies/mL) and therefore should use condoms.

Follow the Advanced HIV Care algorithm below in all patients who appear clinically unstable with any signs or symptoms of:

- TB, cryptococcal meningitis or COVID-19
- PCP, Hepatitis or Cancer
- Opportunistic infections and/or other unstable co-morbidities
- CD4 count <200 cells/µL
- 3rd Trimester of pregnancy without viral load suppression.
- Women with previous history of miscarriage or complications during pregnancy or delivery.

- Abnormal laboratories *(as outlined in Annex 6: ART Nurse Prescribers)*

- Previously documented as having had a severe adverse reaction to ART.
- **ALL CHILDREN < 5 years of age.**

All clinically STABLE patients should immediately be initiated on ART.

5.2 Same Day and Fast Track ART Initiations

Educate patients on the importance of both early treatment and strict adherence. Help them to understand that although they may be healthy now - initiating ART is currently the only way known to prevent the eventual decline of immune function and the development of opportunistic infections.

Immediate initiation of ART will:

- Suppress viral load and protect sexual partners from HIV transmission (U=U).
- Decrease:
  - Mortality and morbidity.
  - Chances of contracting TB and developing cancer.
  - Possibilities of intolerance and toxicities of ART.
  - Chances of treatment failure.
  - Provide the best way to ensure normal life expectancy.

Lack of baseline labs should NOT prevent initiation of ART, if after screening patients are found be well and clinically stable. In these cases, draw baseline labs on the day of initiation, with follow up results returned within 2 weeks. Ensure that contact details are clearly documented in the medical record for follow-up when necessary.

Follow the Clinic Visit Schedule and Laboratory Requirements as outlined Chapter 6.

5.3 Adherence Counseling

The aim of ART is not only to treat viremia, but also to ensure good understanding of the need for strict adherence and attendance at regularly scheduled follow-up visits. Educate and discuss the following topics with all patients initiating ART:

1. For now, there is no known cure for HIV.
2. Taking ART is a life-long commitment and for now, the only guarantee for PLHIV to live normal, happy and healthy lives.
3. **Undetectable = Untransmittable:** With full viral suppression (VL <200 copies/mL), PLHIV **WILL NOT TRANSMIT HIV** to their sexual partners.
4. Before stopping ART for any reason, they should first seek the advice of their healthcare providers.
5. Defaulting from treatment will decrease their chances for remaining disease free.
6. Patients should seek mental health support when their life circumstances cause self-stigma, depression and/or anxiety, suicidal ideation or the desire to stop taking ART.

In addition to adherence counseling, provide patients with information and education regarding:

- Possible ART toxicities
- Positive living and lifestyle modification
- Sexual Reproductive Health
- Pregnancy, contraception and STI management

5.4 ART Initiation & Optimization

Botswana has remained committed to providing more effective and better tolerated ART regimens. This now includes the use of two-drug regimens and long-acting injectable formulations as they become available and affordable.

Availability of long acting injectables within the private sector can precede the public implementation. However, patients who reach the medical aid financial limits for these formulations in the private sector, may be required to return to the use of oral medications once they are transferred back into the public sector.

Use of dual therapy regimens will begin before the end of 2023. Guidance on eligibility and prioritization for switching treatment groups will be communicated. Facilities should not begin switching to dual therapy before they receive official notice detailing instructions. For questions regarding treatment optimization contact an HIV Specialist or the National ART Programme.

Unless instructed and approved by an HIV Specialist for special use, there should no longer be any patients on regimens that contain EFV, NVP or LPV/r in the public or private sectors.

5.4.1 Initiation and On-Going ART Usage

Begin ART as described in Table 14a and 14b below:

Table 14a: Initiation of Treatment Naïve Patients

1st Line Regimen Treatment Naive	1st Line Modifications
TAF-ED 1 tablet OD *Including pregnant women at any gestation*	Intolerance to DTG: TDF+XTC^+Doravirine (DOR) Intolerance to TDF 3TC+DTG *(with approval of an HIV Specialist and following testing for Hepatitis BsAg)*
NOTE: › *All 1st Line patients identified with VL>200 copies/mL after 6 months of ART must follow the **ART Failure Algorithm.*** › *^XTC can be used as either 3TC or FTC* › ***In cases of TB/HIV co-infection, do not use Doravirine***	

Table 14b: 2nd and 3rd Line Regimens

2nd Line Regimen	2nd Line Modifications	3rd Line Regimens
DOR 1 tablet (100mg) OD + DAR/r 2 tablets (400/50mg each) OD	*Intolerance to this regimen must be discussed with an HIV Specialist*	Discuss the 3rd line regimen design with an HIV Specialist

For detailed guidance on switching to Second-Line regimens see Chapter 8.

5.4.2 Simplification to Dual Therapy

Use of XTC+DTG has proven to be non-inferior to triple ART regimens[1,2,3,4] Beginning in 2023, selected patient populations will be switched to dual therapy to reduce long term toxicities often experienced with ART triple regimens. Priority will first be given to patients with intolerance/ toxicities to TDF and TAF regimens, renal insufficiency and chronic kidney disease.Dual therapy eligibility will be expanded to other patient populations as outlined in the 2023 ART Programme Operational Plan.

It is important to note that dual therapy should only be used in patients with full viral suppression VL ‹200 copies/mL (or previously VL ‹400 copies/mL) for at least 2 years.

- Before switching to dual therapy – TEST (or re-test) ALL patients for Hepatitis as outlined in Chapter 6.
- Avoid placing patients with immunological failure on dual therapy.
- If immunological failure has been long-standing and the patient has remained clinically stable, discuss dual therapy treatment options with an HIV Specialist before switching.
- Treat and resolve all OIs or co-infections before switching.
- Monitor LFTs in all patients switched to dual therapy to rule out undiagnosed Hepatitis and the development of a hepatitis flare.

Patients who test positive for Hepatitis must remain on TDF or TAF containing regimens.

Remember to send a Priority Viral Load (PVL) 4-6 weeks after treatment switch. Patients who develop viremias of VL ›200 copies/mL, must return to their original triple therapy regimens. Track these patient's outcomes and discuss with HIV Specialists as needed.

5.4.3 Simplification for Highly Treatment Experiences (HTE) Patients

The majority of HTE patients (those who are taking darunavir/ritonavir containing regimens) have failed two more ART regimens including raltegravir.

- Switch all HTE who maintained complete viral load suppression for greater than 2 years, to the following once a day regimen:
    - **DAR/R 400mg/50mg 2 tablets + TLD (or TAF-ED)**

However, **HTE patients who have not remained suppressed on once-a-day dosing regimens** should return to twice-a-day dosing as follows:

- **AM Dose:** DAR/R 2 tablets 400mg/50mg + TLD (or TAF-ED)
- **PM Dose:** DTG 50mg

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[1] **Rolle, Charlotte-Paige, et. al.,** Sustained Virologic Suppression with Dolutegravir/Lamivudine in a Test-and-Treat Setting Through 48 Weeks. *Open Forum Infectious Disease*. 2023. https:/doi.org/10.1093/ofid/ofad101

[2] **Amor-García MÁ, et. al.** Dolutegravir-Based Dual Therapies in HIV Pretreated Patients: A Real-Life Study in Madrid. *Annals of Pharmacotherapy*. 2022;56(4):401-411. doi:10.1177/10600280211038504

3. Cahn P, et. al. Efficacy of Dolutegravir Plus Lamivudine in Antiretroviral Treatment-Naive Adults With HIV-1 Infection: 96-Week Results From the GEMINI-1 and GEMINI-2 Randomized Clinical Trials. J Acquir Immune Defic Syndr. 2020 Mar 1;83(3):310-318. doi: 10.1097/QAI.0000000000002275. Erratum in: J Acquir Immune Defic Syndr. 2020 Jul 1;84(3):e21. PMID: 31834000; PMCID: PMC7043729.

4. **Jean van Wyk, et.al.** Efficacy and Safety of Switching to Dolutegravir/Lamivudine Fixed-Dose 2-Drug Regimen vs Continuing a Tenofovir Alafenamide–Based 3- or 4-Drug Regimen for Maintenance of Virologic Suppression in Adults Living With Human Immunodeficiency Virus Type 1: Phase 3, Randomized, Noninferiority TANGO Study, *Clinical Infectious Diseases*, Volume 71, Issue 8, 15 October 2020, Pages 1920–1929, https://doi.org/10.1093/cid/ciz1243

Because HTE patients with VL >200 copies/mL may be eligible for compassionate use of newer regimens, they should always be monitored closely. Discuss HTE patients with an HIV Specialist as needed.

Chapter 6
Revised Laboratory, Clinical Visits & Pharmacy Schedules

6.1 Laboratory Considerations

6.1.1 Baseline Laboratories

Every effort should be made to complete baseline laboratory evaluations. However, if laboratory reagents or commodities are not available and after careful medical review including a full physical examination ensuring that patients are free of ANY OIs or other chronic medical conditions:

DO NOT POSTPONE INITIATION OF ART in the absence of baseline laboratory results. For questionable cases, doctors should seek the advice of an HIV specialist. Experienced clinical judgment is always required to initiate patients without baseline laboratory results.

ART nurse prescribers must seek the approval of an experienced HIV clinician before initiating ART without baseline labs for patients who are clinically unstable.

- Follow up in these cases should be made after two weeks of initiation to prevent unnecessary clinical complications.

6.1.2 Expected Lab Turn Around Times

Facilities should expect the following optimal turn-around times for laboratory results:

- Priority Viral Load: 1 week
- Viral Load 2 weeks
- CD4 counts: 3 working days
- Routine Laboratories (i.e., LFT, RFT, FBC): 3 working days
- Serology (i.e., RPR/ TPHA, CrAg, Hepatitis screen): 1 week
- Lipid profile (patients ≥50 years): 1 week
- GeneXpert 24 hours
- Infant PCR 72 hours

If your facilities are experiencing serious laboratory delays, inquire first at your local laboratory and if the problem cannot be resolved there, escalate your inquiry to National Laboratory.

6.2. Clinical Visit Schedule

6.2.1 Clinical Visits

Tables 17 and 18 below outline the revised clinical visit schedule for clinically stable patients. Those who remain clinically stable and virologically suppressed, may be placed on Q6-monthly appointments. However, once they become ill, default or experience virological failure, they should be monitored more closely at the discretion of their physicians.

6.3 Pharmacy Multi-Month Dispensing (MMD)

All ART facilities should provide 3 Month -MMD for all clinically stable patients. Six-month MMD should be reserved for special circumstances such a foreign travel and education. Exceptions should be requested directly to ART Programme Manager at the Ministry of Health.

6.4. Revised Laboratory Schedule

For **Triple Therapy Regimens:**
TLD, TAF-ED, TLD + DAR/RIT, TRU+DOR, TRU+ATV/r, ABC+3TC+DTG Regimens

Table 15: Triple ART Regimen Laboratory Schedule.

Test	Baseline *(within 3 months prior to initiation)*	1 month	3 months	6 months	12 months	Thereafter
VL (Adults & Adolescents)			X	If not suppressed at 3 months	X	**Q6 months** (unless LV › 200 follow Tx Failure Algorithm)
Pregnant Women must complete VL testing during each trimester and at Q3 months during breast feeding.						
VL Pediatrics ‹10 years		X	Q3 months thereafter Until 10 years of age			
CD4	X		X	If not ›200	X	**Q12 months** unless CD4 ‹200 then, as often as clinically indicated
FBC	X		If anemic		X	As clinically indicated Q6 months
Electrolytes	X			X		
AST/ALT	X		X	If LFTS are elevated	X	
CR & CRCL Urea	X	X	X	X	X	Q6 Months
RPR	X During Pregnancy at BL and 34-36 wks gestation at ANC					As clinically indicated
Random GLUCOSE	X If elevated, then complete Fasting Glucose		For DM Q3 months Hgb1AC			Without DM Fasting Glucose Q12 Months
Hepatitis B Virus	X					As clinically indicated
Cholesterol › 50 years	X			X		Q6 months thereafter

Laboratory Schedule for DUAL Therapy Regimens:
3TC+DTG, DOR+DAR/r, DTG+DAR/r, ATA/r+DTG

Table 16: Dual ART Regimen Laboratory Schedule

1st Year on Dual Therapy	At the time of Switch	4 -6 weeks Post Switch	3 months	6 months	After 12 months Post Switch
VL	X If not within 3 months	X	X	If not suppressed at 3 months	Q6 months, if clinically stable Otherwise Q4
CD4	X		X	Advanced HIV Care, CD4 <200	Q12 months Or as clinically indicated
FBC	X		Q3 until anemia resolved		ACI
AST/ALT	X		X		Without DM Fasting Glucose Q12 Months
Fasting GLUCOSE	X If elevated, complete HgbA1C		If DM Q3 months		Without DM Fasting Glucose Q12 months
CR & CRCL	X		X	X	Q6 months Year One
RPR	X				As clinically indicated
Hepatitis	Screen before Switch				
Cholesterol & Triglycerides Q6 months for PLHIV with HTN, DM, CA, Obesity or > 50 years.					

Table 17: Clinic Visit Schedule for Initiation and Follow Up Care of STABLE PATIENTS
(Adolescents, Naïve and Tx switch)

Clinical Condition: STABLE		1 Month post ART initiation or Tx Switch	3 months post ART initiation or Tx Switch	6 months Post ART Initiation or Tx Switch	
Initiations - CD4 >200 - No unstable OIs or comorbidities Tx Switch VL <200 copies/mL (if already on ART)	SAME DAY INITIATION or FAST TRACK	DURING YEAR ONE			Q6 months thereafter

Table 18: Clinic Visit Schedule for Initiation and Follow Up of Advanced Care Patients
(Adult, Adolescents & Children) including patients with viremia and defaulters.)

<table>
<tr><td rowspan="2">Clinical Condition: Advanced HIV
Clinically UNSTABLE</td><td rowspan="2">Initiate/ Reinitiate ART
If CrAg & TB LAM are negative:
SAME DAY or FAST TRACK
(Initiate optimally within 3 days)</td><td rowspan="2">Follow up visits as clinically indicated or as follows:</td><td>1-2 weeks after 1st follow up visit</td><td>Q1-3 months</td><td>Q3 m for the rest of the 1st year</td><td rowspan="2">Once stabilized Every Q6 months thereafter</td></tr>
<tr><td>-CD ‹200
- Reports to be ill
- Uncontrolled comorbidities
- OIs
- VL ›200 copies/mL</td><td colspan="3">DURING YEAR ONE</td></tr>
</table>

CHAPTER 7
Advanced HIV Care & Treatment

7.1 Advanced HIV Care (AHC)

Managing patients who present with life-threatening opportunistic infections, serious co-morbidities and/or CD4 counts below 200 cell/ µL, requires intensified clinical screening, specialized care and close monitoring. Reducing mortality and morbidity in these patients by providing specialized HIV care has become a priority in Botswana and throughout the world.

7.2. Screening, Diagnosis & Treatment Algorithms

Clinically unstable patients with CD4 ‹200 cells/µL or who have defaulted from ART, have suspected or confirmed serious co-morbidities and/or OIs, should undergo the following at ART initiation/re-initiation:

- Full Physical Examination (with particular emphasis on hepatosplenomegaly & lymphadenopathy)
- CD4 Count with full clinical assessment.
- PVL (for all re-initiations)
- TB Urine LP LAM test
- CrAG LFA Rapid Test
- Gene Expert Test *(see Annex 6, Table 2: Interpretation of Xpert Results)*
- Chest Xray and Rapid COVID-19 - as clinically indicated.
- Cancer prevention screening, including cervical, breast and prostate.

Closely monitor and track results of all AHC patients. Questions regarding HIV Advanced Care should be directed to an HIV Specialist as needed *(see Annex 2: HIV Specialist Directory)*.

7.3 Diagnosis & Treatment of Cryptococcal Meningitis

Research from Botswana shows that 6% 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 200 cells/µL with serum or plasma cryptococcal antigen (CrAg) tests and treat them according to the guidelines below.

Serum CrAg may also be performed in people with CD4›200 on clinical grounds (if concerned about HIV-related meningoencephalitis).

7.3.1 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. Lack of 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 (LP) in all PLHIV suspected to have cryptococcal meningitis.

Although considered an "opt-out" procedure, a lumbar puncture should be considered an emergent, 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

- 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/or other focal neurologic signs. However, in all other situations, CT is not a requirement for a lumbar puncture.
- Complete the following on CSF:
  - Cryptococcal antigen test (CrAg)
  - Cryptococcal culture (plus India ink stain if no CrAg available)
  - Cell count, differential, MCS, protein and glucose.

In cases displaying lymphocytic meningitis and negative India ink, CrAg and culture, the most likely diagnosis is TB meningitis. Perform Xpert Ultra MTB/RIF (GeneXpert) on CSF and TB culture. Begin treatment for TB meningitis and discuss with an HIV/TB specialist.

7.3.2 Treatment: Antifungal Therapy

Treat Adults and Children for Cryptococcal Meningitis as follows:

Table 19: Antifungal Treatment of Cryptococcal Meningitis

Follow These Steps:	Adults	Paediatrics
1. **Induction** for 2 weeks	*$**Liposomal Amphotericin** (AMBISOME): 10 mg/kg SINGLE DOSE IV (day 1 only) PLUS *Flucytosine 100mg/kg/day PO in 4 divided doses (14 days) *(per dose: 25mgs/kg)* PLUS **Fluconazole:** 1200 mg PO daily (14days)	*$**Liposomal Amphotericin** (AMBISOME): 10 mg/kg SINGLE DOSE IV (day 1 only) PLUS *Flucytosine 100mg/kg/day PO in 4 divided doses (14 days) *(per dose: 25mgs/kg)* PLUS **Fluconazole:** 12 mg/kg PO daily (14 days; maximum of 800 mg daily)
2. **Consolidation** for 8 weeks	**Fluconazole:** 800 mg PO daily	**Fluconazole:** 6-12 mg/kg PO daily (maximum of 800 mg)
3. **Maintenance** Until CD4 count remains ›200/15% for 6 months	**Fluconazole:** 200 mg PO daily	**Fluconazole:** 6 mg/kg PO daily (maximum of 200 mg daily)
INITIATE, RE-INITIATE OR SWITCH ART 4-6 WEEKS AFTER INITIATION OF ANTIFUNGAL THERAPY		

*** If liposomal amphotericin is not available use:** Amphotericin B Deoxycholate 1 mg/kg/day + flucytosine 100 mg/kg/day in 4 divided doses (both for 7 days) in both adults and children, followed by fluconazole 1,200 mg daily for 7 days in adults, or fluconazole 12 mg/kg per day for 7 days in children (up to a maximum of 800 mg daily), followed by consolidation and maintenance treatment as above.

***If flucytosine is not available, use:** Amphotericin B Deoxycholate 1 mg/kg/day + fluconazole (1,200 mg daily in adults or 12 mg/kg per day up to a maximum of 800 mg in adolescents and children) for 14 days, followed by consolidation and maintenance treatment as above.

***If both Amphotericin B and Liposomal Amphotericin are not available for adults, use:** Flucytosine 100 mg/kg/day in 4 divided doses + Fluconazole (1,200 mg daily in adults or 12 mg/kg per day up to a maximum of 800 mg in adolescents and children) daily for 14 days, followed by consolidation and maintenance treatment as above.

For patients with CD4‹200 found to have positive cryptococcal antigen test:
Evaluate for symptoms and signs of cryptococcal meningitis. In all symptomatic patients and in asymptomatic patients if LP is available and patient is willing to undergo the procedure, perform LP and test for cryptococcal meningitis. If positive CSF CrAg (or India ink) treat as above. If asymptomatic or negative CSF, treat with oral fluconazole 1,200 mg for 2 weeks, followed by consolidation and maintenance treatment as above.

[$]See Appendices for Liposomal Amphotericin reconstitution.

7.3.3 Toxicity Management

Ensure pre-hydration (1 L Normal Saline + 20 mmol KCL) and post-hydration with each dose of amphotericin regardless of amphotericin formulation (liposomal or deoxycholate).

Daily oral supplementation with Slow-K 1,200mg BD and Slow-Mg 1,070mg OD, continue during amphotericin therapy and for 2 days after IV amphotericin therapy has finished. Do not give IV KCL or Slow-K if K^+› 5.0.

If renal toxicity occurs, dose flucytosine as per guidance in the appendices. For fluconazole, if creatinine clearance reduces to **‹ 50 ml/minute** give same initial dose but reduce subsequent doses by 50%.

For bone marrow toxicity from flucytosine, use guidance in the appendices. Bone marrow toxicity is very rare at the doses used to treat cryptococcal meningitis.

7.3.4 Special Considerations with ART

- 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 TLD (and TAF-ED) can be continued.
- Fluconazole and flucytosine should ideally be avoided in the first trimester of pregnancy or during breastfeeding. However, the benefit of these drugs in patients with cryptococcal infection will almost always outweigh the risks.
- **Discuss cases of women who develop cryptococcal meningitis during their first trimester of pregnancy with an HIV specialist.**

7.3.5 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 or presence of symptoms suggestive of raised ICP.

- Drainage of CSF should be performed to normalize ICP to <20 cm H2O. Ensure that the patient has had **2 consecutive normal ICP measurements** prior to stopping therapeutic LPs.
- Mannitol has no effect on raised ICP and acetazolamide and dexamethasone are both associated with harm.
- Shunts and/or drains are not routinely recommended as they are associated with high rates of nosocomial sepsis.

(See detailed guidance in Annex 7: Raised ICP Management)

7.3.6 Cryptococcal Meningitis Relapse

This may occur if there was inadequate induction and/or non-adherence and/or fluconazole resistance. The patient will present with recurrence of symptoms suggestive of cryptococcal meningitis.

- **CSF findings:** Positive neoformans/gatti culture
- **Management:** Re-initiate induction therapy as per Table 19 above. Defer ART to 4-6 weeks post induction if the patient has not been initiated.

CrAg tests can remain positive for a year or more after effective treatment for cryptococcal meningitis, so a positive CrAg does not necessarily indicate a reactivation of cryptococcal disease in the context of symptom recurrence.

7.3.7 Cryptococcal Meningitis IRIS

May present as unmasking IRIS in newly initiated patients or paradoxical IRIS in patients previously treated from cryptococcal meningitis. Unmasking IRIS usually occurs from 2 weeks to 3 months after ART initiation. Paradoxical IRIS is characterised by raised ICP, possibly high CSF protein and WCC and negative culture on background of good adherence. The risk is reduced if effective antifungal induction was given, and ART started between 4-6 weeks.

Management:

- Re-initiate induction therapy as per Table 19 above.
- Continue ART.
- Investigate with LP to exclude culture positive cryptococcal relapse and other causes of meningitis.
- Only give steroids if culture-positive relapse is excluded and unable to control symptoms and raised ICP.

7.3.8 Cryptococcal Meningitis Among Children

Given the lack of data of cryptococcal meningitis in children, current recommendations for the treatment 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.

7.4 TB/HIV Co-Infection

Shortened courses of ATT for both drug sensitive (DS) TB and Multidrug resistance (MDR) TB are now known to be noninferior to previous longer course regimens and are endorsed by the Botswana Ministry of Health. Revised guidelines for these regimens will be made available through the Botswana National Tuberculosis Programme (BNTP). In the meantime, clinicians should continue to follow the previous treatment recommendations for DS TB, as outlined below.

Clinical evidence shows that early ART initiation reduces the risk of death in TB/HIV patients. This is particularly important at low CD4 counts. ART naïve patients (or those restarting treatment for

any reason) with low CD4 counts should start ART as soon as they are tolerating ATT and at the 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 to decrease mortality.
- All TB/HIV co-infected patients must receive prompt referral and timely follow-up in HIV care facilities.
- Always provide counseling and social support and refer for home-based care as necessary.

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

Routinely screen for TB in all places where PLHIV receive medical care, including: ART clinics, STI clinics, hospital wards, PMTCT facilities & HIV Testing & Counseling Centers.

7.4.1 Intensified Case Finding (ICF)

ICF involves promptly detecting TB by identifying the presence of:

- Cough of any duration
- Fever, night sweats, weight loss
- Evidence of lymphadenopathy.
- Detectable HIV viral load
- In children: Decreased playfulness

Any one of the above symptoms makes one a presumptive TB case and should be investigated for TB. All presumptive TB cases should have a sputum sample collected for Gene Xpert testing.

Remember: A detectable viral load in a previously suppressed patient may be the first sign of TB disease. While patients must be assessed for other causes of ART failure such as adherence, all failing patients must be carefully screened for 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, always ask about TB exposure in the household as part of the symptom screen. Asymptomatic children with TB contacts are candidates for IPT *(see Section 9.2: Prevention of TB & ANNEX 7: Algorithm to Diagnose TB in Children <12 years)*

7.4.2 LF-LAM/TB-LAM

Is a point of care non-sputum test for detecting all TB, including children. It should be done for the following patients:

- All HIV infected presumptive TB cases with CD4 cell count <200.
- Inpatients and outpatients with HIV, who are seriously ill – regardless of the CD4 count or if the CD4 count is unknown.

7.4.3 Indications for Culture and DST:

- Confirmed TB cases.
- All TB diagnosed cases diagnosed by Gene Xpert with or without Rifampicin resistance.
- All TB cases diagnosed through smear microscopy when Gene Xpert is not available.

7.4.3a Paucibacillary Disease (especially in children)

- Samples collected from extra pulmonary sites in patients with suspected EPTB.

- **Children:** All children should have 2 samples collected (1 for Gene Xpert testing and 1 for TB C/DST.
- All TB presumptive PLHIV with 2 negative Gene Xpert results, in particular those with advanced immunosuppression (i.e., CD4<200 cells/µL).

- All 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.

7.4.3b. Other Indications

- Patients with bloody sputum should have samples sent for TB Culture and DST as such specimens cannot be performed on Gene Xpert.
- Patients who are still smear positive after 3 months of treatment.
- Patients who are smear positive at the end of treatment.

7.4.4 Empiric Treatment

Empiric treatment with ATT may be required in clinical cases when laboratory diagnostics are not available or inconsistent with clinical symptoms. **Exercise a low threshold for empiric treatment in the following cases:**

- In very ill patients with signs and symptoms of TB.
- Abdominal ultrasound displaying lymphadenopathy.
- Cardiac ultrasounds displaying pericarditis with or without pericardial effusion.
- Persistent fever despite broad spectrum antibiotics.

Ideally, commit to 6 months of empiric treatment, except in refractory cases with lymphadenopathy, which may be lymphoma and must be ruled out.

7.4.5 ART and ATT Co-Administration

For adults & adolescents already on ART who develop TB, follow Table 20 below:

Table 20: ART & ATT Regimens

ART Regimen	ART Adjustment for ATT
TRU/DTG TAF-ED/DTG CBV/DTG ABC/3TC/DTG	**Do not double dose DTG in Adults** *Only double dose DTG in Children, Adolescents & Pregnant Women*
CBV/ATV/r TRU/ATV/r ABC/3TC/ATV/r	1. Stop ATV/r or LPV/r. 2. Maintain original NRTI backbone 3. In cases of ART failure, discuss with an HIV/TB Specialist
All DOR containing regimens, Highly treatment experienced patients on DAR/r and NRTI backbone regimens	Discuss with HIV/TB Specialist
Discuss patients who cannot tolerate DTG regimens with an HIV/TB Specialist	

All HIV patients should begin ART as soon as possible.

7.4.6 ART Naïve Patients Who Develop TB

Always initiate ATT first, followed by ART as soon as possible but no later than 2 weeks.

- Start ART as soon as the patient is tolerating ATT when CD4 counts are ‹100 cells/µL.

7.4.7 Patients with Suspected Neurological Involvement or Deranged ALT

Exercise caution with severely immunosuppressed patients (e.g., CD4 counts ‹50 cells/µL) with suspected neurological involvement or deranged LFTs.

- Closely monitor these patients for hepatitis and worsening of TB due to IRIS (seek advice from TB/HIV specialist as necessary).

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

Initiate ART in naïve patients as indicated in Table 21 below:

Table 21: HIV Treatment Regimens for Adult TB/HIV Patients while taking ATT

Line of Therapy	Drug Regimen
First-line including: ▪ Adults ▪ Pregnant women ▪ Adolescent (›25kg)	**TAF-ED 1 tablet OD**

Note: *Contact TB/HIV specialist for assistance with ART intolerance or medication stock-outs. TLD may be used an alternative first line.*

Remember:

- Patients of all ages with active TB must be started on CTX prophylaxis.
- If at the end of ATT, the CD4 counts remain ‹200 cells/µL, continue CTX.
- **All PLHIV healthcare workers caring for patients with TB and suspected TB - especially MDR-and XDR-TB, must always observe respiratory isolation precautions.**
- **It is no longer necessary to double dose DTG while taking ATT.**

7.4.9 Special Considerations for TB in Pediatric Patients

All recommended Pediatric ART regimens are safe with ATT

The risk of developing TB disease following infection is mainly determined by:

- **History of a recent TB contact:** Adult or adolescent with PTB.
- **Age**: Risk of developing active TB is highest in very young children (‹ 3 years).
- **Time since exposure/infection**: Most children who develop TB disease do so within the first year after latent infection.
- **Immune status:** Conditions that suppress the immune system make disease more likely; these include HIV, severe malnutrition, and immune suppressive therapy such as corticosteroids.

7.4.9a TB Diagnosis in Children

Microbiologic confirmation is challenging, as sputum samples are difficult to obtain, especially in young children. However, most pediatric TB cases will be detected by a thorough clinical evaluation and stool samples.

7.4.9b Hypersensitivity Phenomena

This represents early clinical evidence of the immune system response to M. tuberculosis infection. The following may occur 8-12 weeks after a child is infected:

Common:

- TST conversion

Less common:

- Erythema nodosum: painful nodules usually on the shins
- Phlyctenular conjunctivitis: red nodule on the eye with conjunctival injection
- Polyarthritis

(See ANNEX 7: Diagnostic Algorithm for Pulmonary TB in Children ≤ 12 years)

Contact a TB/HIV specialist in cases of infants <1 month old, or those on salvage or history of unusual ART regimens.

7.5 Nonresponse to ATT

All patients who fail to respond to standard ATT (i.e., do not seroconvert or continue to clinically deteriorate) must have sputum sent for TB culture and repeated GeneXpert for suspected MDR-TB.

A major breakthrough in the treatment of MDR-TB is use of Bedaqualine, Pretomonid, Linezolid, Moxifloxacin (BPaLM) regimen, which requires only 6 months of treatment with 95% cure rate. Guidelines on the use of improved regimens will soon be made available through the BNTP.

7.6 Screening, Diagnosis & Treatment for Viral Hepatitis

The diagnosis and treatment of viral hepatitis has become an increasingly urgent global health concern because of its high mortality and morbidity. In response, Botswana has endorsed the WHO target of hepatitis elimination. Therefore, all PLHIV, particularly those who are switching to dual therapies and pregnant women, must be tested and have their hepatitis status well-documented in their medical records. The full recommendations for the diagnosis and treatment of hepatitis are outlines in Table 22, below. Currently, not all the laboratory tests listed are available within the public sector, however these tests are available in the private sector. Once these labs are offered within the public sector facilities will be notified.

Prompt diagnosis and treatment of viral hepatitis is required to prevent morbidity and mortality in PLHIV, who are at higher risk of developing cirrhosis and liver cancer. This is particularly true for all key populations and those who engage in condomless sexual activities and other high-risk sexual behaviors.

Screen all PLHIV for Hepatitis at the following times:

- Baseline before ART initiation.
- Before switching to dual therapies (oral or injectable).
- With clinical signs and/or symptoms of viral hepatitis.

Screen sexual partners, children, other family members and close household contacts of those diagnosis with viral Hepatitis B infection.

Table 22: Hepatitis Screening & Treatment in PLHIV

<table>
<tr><th></th><th>Test</th><th>Results</th><th>Action</th></tr>
<tr><td rowspan="4">Baseline Screening
at ART initiation

When Hepatitis is clinically suspected screen for both HBV and HCV by adding:</td><td rowspan="3">HBV surface antigen (HBsAg)
AND
HBV core antibodies (anti-HBc)
(currently only available in the private sector)</td><td>If one or both results are negative (regardless of CD4 count):</td><td>Vaccinate for Viral Hepatitis</td></tr>
<tr><td>If either anti-HBsAg
or
anti-HBc are positive:</td><td>Do not Vaccinate</td></tr>
<tr><td>If HBsAg is positive

And/or

If anti-HBc is positive with elevated transaminitis
(or clinically suspected)</td><td>▪ Send: HBV viral load
▪ Screen for HCV
▪ Monitor LFTs
▪ Initiate: TDF or TAF based regimen
(Treatment is lifelong)

And additionally, screen for:
-HBV e antigen (HBeAg) &
-HBV e antibodies (anti-HBe)
-Hepatitis Delta (HDV)</td></tr>
<tr><td>HCV antibodies
(Anti-HCV)</td><td>If anti-HCV is positive</td><td>Send: HCV viral load and Refer to hepatology/GI for HCV treatment</td></tr>
<tr><td>At Switch to Dual Therapy</td><td>HBsAg</td><td>HBsAg is positive</td><td>Maintain Triple Therapy with a TRU or TAF containing ART*</td></tr>
<tr><td colspan="4">* To avoid a hepatitis flare: If for any reason TDF/XTC or TAF/XTC must be stopped or modified, discuss the case with an HIV Specialist and GI Specialist to manage reactivation of HBV and avoid hepatocellular damage.</td></tr>
<tr><td colspan="4">Instruct all HBV & HCV patients (regardless of HIV status) to NOT stop TRU or TAF without discussing this with their health care providers.

PLHIV who test positive for viral hepatitis B or C: ARE NOT ELIGIBLE FOR ORAL OR INJECTABLE DUAL THERAPY ART REGIMENS</td></tr>
</table>

- All PLHIV diagnosed with viral hepatitis should ideally be reviewed by hepatology/GI clinic for monitoring and treatment recommendations.

- All adults, adolescents and children with chronic hepatitis B and clinical evidence of compensated or decompensated cirrhosis *(or cirrhosis based on APRI score >2 in adults – see below)* should be treated, regardless of ALT levels, HBeAg status or HBV DNA levels.
- Monitor for HBV treatment response/disease progression, every 12 months (ALT, renal function, HBV DNA viral load) or every 6 months depending on disease stage, when available.

Determine the status of possible liver damage using the APRI Score (AST/Platelet Ratio):

- If score is equal or less than 0.5 = Normal or minimal scarring
- If the score is above 0.5 = Fibrosis is likely

- HIV negative pregnant women who test positive for HBV infection (HBsAg positive) follow algorithm outlined in Table 22, above.

Note for HIV Negatives: **HBV positive pregnant women, must have** all sexual partners, children and other family members, and close household contacts for HBV infection.

7.6.2 Other Causes of Hepatitis

Screen all patients with transaminitis for alcohol abuse and other causes of liver disease including:

- Cardiac or renal disease
- Autoimmune, genetic or metabolic liver disease (e.g., diabetes, genetics, obesity and hemochromatosis)
- Drug induced hepatotoxicity

Screen all patients with persistent clinical signs and symptoms of Liver Disease (i.e., masses, cirrhosis, elevated transaminitis, etc.) These cases should be promptly referred to a medical specialist and/or hepatology/GI clinic. Be sure to exercise care to track and follow up all such patients.

In cases of Obesity, Metabolic Syndrome, DM and persistent elevation of ALT

- Consider Non-Alcoholic Fatty Liver Disease (NALFD).
- Order abdominal ultrasound and refer to hepatology/GI clinic as required.

7.6.3 Treatment for Hepatitis C

- Consider prescribing treatment with Direct Acting Antiviral (DAA) agents
- Remember: Regardless of HIV status – HCV treatment is equally effective.
- Always refer to hepatology/GI clinic for treatment and follow up.

Questions regarding other causes or complications of hepatitis should be directed to hepatology/GI clinic.

7.7 Immune Reconstitution Inflammatory Syndrome (IRIS)

IRIS is a potential complication that can occur following the initiation of ART, when improvement of immune function is accompanied by the worsening of a current opportunistic infection or the unmasking of a latent or recent one. IRIS presents as a paradoxical worsening of clinical status despite favorable CD4 and VL responses. IRIS occurs most frequently with low CD4 counts (<50 cells/µL) at baseline or at re-initiation and with rapid VL decline and robust immune reconstitution.

- IRIS most commonly occurs in the setting of underlying mycobacterial infections (e.g., TB, Cryptococcal infections and herpes virus infections (HSV, VZV, CMV, KS). Almost all other OI have also been associated with IRIS.
- Systemic steroids can be given when the inflammatory damage at the site of involvement severely impairs organ function and becomes life-threatening (e.g., upper respiratory obstruction from lymphadenopathy due to TB or KS).

7.8 Description & Treatment of Other Opportunistic Infections

Table 23: OIs (Adapted from CDC HIV Clinical Care Guidelines and EACS Guidelines 2021)

OI	Description
Candidiasis	▪ Caused by infection with a fungus called *Candida Albicans.* ▪ Affects the skin, nails, and mucous membranes, especially on the vagina and the mouth (can present as streaky hemorrhagic fpatches and fine white deposits, the tongue may develop the appearance of "raw beef"). ▪ Can cause severe or persistent infections in the mouth or vagina, or when it develops in the esophagus (causing dysphagia) or lower respiratory tract, such as the trachea and bronchi.
	Treatment: Fluconazole 200mg PO OD x 5 days, *(Esophagitis: 400mg loading dose, then 200mg x 10-14 days)*
Invasive cervical cancer	▪ Starts at the cervix and becomes invasive. ▪ Can be prevented by having regular examinations and pap smear of the cervix.
	Treatment: Immediate initiation of ART & referral to oncology
Cryptococcosis	▪ Caused by infection with *Cryptococcus neoformans.* ▪ Typically enters the body through the lungs and can cause pneumonia. ▪ Usually affects the lungs or the CNS, but it can also affect other parts of the body.
	Treatment: See Section 7.3, page 49
Cytomegalovirus (CMV)	▪ Can infect multiple parts of the body and cause pneumonia, gastroenteritis (especially abdominal pain caused by colitis), encephalitis, and sight-threatening retinitis. ▪ Can worsen vision over time. CMV retinitis is a medical emergency because it can cause blindness if not treated promptly.
	Treatment: Ganciclovir 5mg/kg IV BD x 3 weeks, as condition improves may be switched to PO Valganciclovir 900mg BD for the duration of the treatment (a total of 3 weeks)

	In cases with visual impairment make an urgent referral to Optho and IV Ganciclovir will be required. In cases with mild retinitis, Valgancicolvir 900mg PO BD with food for 2-3 weeks.
Diarrhea	• Enters the body through contaminated food or water. Symptoms include watery (and/or bloody) diarrhea, fever, headache, abdominal pain, vomiting, weight loss and wasting. • Commonly caused by: Giardia, Shigella, Salmonella, Amoebiasis • **Pathogens include:** Cryptosporidium, Cytomegalovirus (CMV) Microsporidia & Cystoisospora *(formerly known as isosporiasis)*.
	AdultTreatment: Initiation ART, rehydration and supportive care Cystoisosporiasis: Cotrimaxazole 1600/320 mg (two DS Tabs PO BD) x 10 days, increase to up to 3-4 weeks if worsening or persisting symptoms. **Pediatric Treatment:** **NOTE: Adults and children with signs of dehydration may need hospital admission for IV rehydration.** Exercise caution as hospitalization may be necessary - rehydration is key.
Wasting Syndrome	Involuntary loss of >10% of body weight while experiencing diarrhea or weakness and fever for more than 30 days. Treatment is primarily ART, contact HIV Specialist as required.
Encephalopathy	▪ A brain disorder that can occur as part of acute HIV infection or result from chronic HIV infection. ▪ Exact cause is unknown, but thought to be related to infection of the brain with HIV and resulting inflammation
	Treatment: Immediate initiation of ART
Herpes simplex virus (HSV)	• A common virus usually acquired sexually or passed from mother-to-child during birth. • In most people with healthy immune systems, HSV is usually latent. • Stress, trauma, menses, other infections, or suppression of the immune system, (such as by HIV), can reactivate the latent virus and symptoms can return. • Causes painful cold sores (fever blisters) in or around the mouth, or painful ulcers on or around the genitals or anus. • With severely damaged immune systems, it can cause infection of the bronchus, lungs, esophagitis and brain (temporal lobe encephalitis).
	Treatment: Acyclovir 400-800mg PO BD x 7-10 days Consider daily suppressive *therapy for* those with severe and/or recurrent outbreaks: *Acyclovir 400mg PO OD daily*
Histoplasmosis	• More commonly seen in South Africa • Caused by the fungus *Histoplasma and* most often develops in the lungs. • Produces symptoms similar to the flu or pneumonia. • Can develop into a very serious progressive disseminated histoplasmosis. This can last a long time and spread to other parts of the body.

	Treatment: **Liposomal Amphotericin 3mg/kg x 2-4 weeks followed by: Itraconazole 200mg TDS x 3 days, then 200mgs BD x 12 weeks** (respiratory complications and hypoxemia may need prednisolone 0.5-1mg/kg/day in the first two weeks.
Kaposi's sarcoma (KS)	• Caused by a virus called Kaposi's sarcoma herpesvirus (KSHV) or human herpesvirus 8 (HHV-8), which causes small blood vessels to grow abnormally and can occur anywhere in the body. • Appears as firm pink or purple spots on the skin that can be raised or flat. • Can be life-threatening when it affects organs inside the body, such as the lung, lymph nodes, or intestines.
	Treatment: Initiation of ART and immediate referral to oncology
Lymphoma	• Cancer of the lymph nodes and other lymphoid tissues. • Many types, such as non-Hodgkin lymphoma and Hodgkin lymphoma are particularly associated with HIV.
	Treatment: Initiate ART and immediate referral to oncology
Tuberculosis (TB)	• Caused by *Mycobacterium tuberculosis*. • Airborne. • Can infect multiple sites, lungs in particular. • Common extrapulmonary include, meninges, lymph nodes, bone. • Symptoms include cough, tiredness, weight loss, fever, and night sweats.
	Treatment: **See Section 7.4: TB/HIV Co-Infection**
***Mycobacterium avium*complex (MAC)**	• Caused by different strains of mycobacterium: *Mycobacterium avium*, *Mycobacterium intracellulare*, or *Mycobacterium* kansasii, *some of which live* in soil and dust particles. • Infections can be spread throughout the body becoming life threatening with weakened immune systems.
	Treatment: **Clarithromycin 500mg BD x 12 months** **Ethambutol 15mg/kg OD x 12 months** *Monitor for the development of ocular toxicity*
***Pneumocystis* Jirovecil pneumonia (PCP)**	• Lung infection caused by the fungus *Pneumocystis jirovecii and* occurs with weakened immune systems. • Signs include: difficulty breathing, high fever, and dry cough, lowered PO2, tachypnea.
	Treatment: TMP-SMX 1,200/240mg (3 DS tablets) PO TDS x 3 weeks
Pneumonia Community Acquired	• Can be caused by bacteria, viruses, and fungi. • Symptoms include: cough (with mucous), fever, chills, and dyspnea. • With weakened immune systems the most common and life-threatening cause is an infection with the bacteria *Streptococcus pneumoniae*, also called *Pneumococcus*. • PLHIV should receive a vaccine to prevent *Streptococcus pneumoniae.*

	Treatment: Mild to Moderate – prescribe oral antibiotics: Amoxicillin 500 mg PO TDS (or 1 gram BD) x 5 days. If penicillin allergy: Doxycycline 200 mg stat, followed by 100 mg BD x 5 days.If poor response or atypical pneumonia suspected and in severe cases add: Azithromycin 500mg OD x 5 days, consider a loading dose of 1gm followed by 500 mg OD x 4 days In severe cases begin Augmentin 1 gram PO BD x 5 days May require IV antibiotics
Progressive multifocal leukoencephalopathy (PML)	• Rare brain and spinal cord disease caused by the JC virus. • Seen almost exclusively in severely damaged immune systems. • Symptoms include loss of muscle control, paralysis, blindness, speech problems, and an altered mental state. • Often progresses rapidly and may be fatal.
	Treatment: **Initiate ART immediately, discuss with HIV Specialist as needed.**
***Salmonella* septicemia**	• Typically contracted by eating or drinking contaminated food or water. • Salmonellosis can affect anyone and usually causes nausea, vomiting, and diarrhea. • *Salmonella* septicemia is a severe form of infection in which the bacteria circulate through the whole body and exceeds the immune system's ability to control it.
	Treatment: Hospital admission for IV antibiotics
Toxoplasmosis	• Caused by the parasite *Toxoplasma gondii*, carried by warm-blooded animals including cats, rodents, and birds, released in their feces. • Developed by inhaling dust or eating contaminated food. • Can also occur in commercial meats, especially red meats and pork, but rarely poultry. • Infection can occur in the lungs, retina of the eye, heart, pancreas, liver, colon, testes, and brain. • Although cats can transmit toxoplasmosis, litter boxes can be changed safely by wearing gloves and washing hands thoroughly with soap and water afterwards. • All raw red meats that have not been frozen for at least 24 hours should be cooked through to an internal temperature of at least 150°F.
	Treatment: **CTX 960 mg per each 10 kgs of weight x 3 weeks**
Varicella Zoster Virus	• Typical appearance of chickenpox & herpes zoster
	Treatment: **Acyclovir 800mg 5 times a day for minimum of 10 days**

7.9 Mental Health

Mental Health is the state of emotional, psychological, and social well-being that enables one to make healthy life choices and establish and maintain supportive relationships. Major life changes such as

divorce, chronic illness, death of a loved one, unplanned pregnancies and biological/genetic factors can precipitate mental health challenges. PLHIV are at greater risk for developing mental health conditions, particularly anxiety and depression, as they routinely cope not only with stigma and discrimination, but the neurological effects of HIV infection itself.

Take time to thoroughly evaluate the mental health status of all PLHIV regardless of their age, especially those who present with clinical complications such as failure of ART.

7.9.1 Evaluation & Management of Depression & Anxiety

Clinical Depression is not only sadness but can also be a cyclical biochemical disorder causing a reduction of the brain's serotonin availability. It can be associated with signs and symptoms including, but not limited to, slowed metabolism, appetite and sleep disorders, fatigue and exhaustion. Hormonal, cognitive and emotional dysfunction can also occur.

Screen patients suspected of depression for:

- Loss of concentration, motivation and decisiveness
- Emotional lability, anger, over sensitivity, uncontrollable disproportional reactions.
- Excessive feelings of guilt, grief or worthlessness
- Family history of depression, anxiety or other mental health disorders
- Previous history of neurological dysfunction or infection
- Excessive alcohol and/or recreational drug use
- Suicidality and/or self-harm (particularly adolescents)

Anxiety can occur with or without clinical depression. Clinicians should probe to identify signs and symptoms of anxiety, which often present physiologically as social anxiety, panic attacks, fight/flight reactions and/or post-traumatic stress disorder (PTSD).

Screening should also include:

- Episodes of excessive worry and/or fear disproportional to events.
- Stress, muscle tension, irritability
- Palpitations, breathlessness, lightheaded & dizziness, GI distress
- Insomnia or hypersomnia
- Abnormal loss or gain of appetite, poor diet
- Excessive use of stimulants (caffeine: tea, coffee, fizzy drinks, etc.)
- Other clinical conditions such as: neurological disorders, hypothyroidism, hypogonadism, Cushing's syndrome, Vitamin B 12 deficiency and/or recreational drug use.

7.9.1a Treatment for Depression & Anxiety

Treatment should be based upon severity. Medications should be used in combination with counseling whenever possible for improved long-term outcomes. Individual and group counseling can be recommended, in addition to referral for spiritual support, prayer and meditation. *(see section 9.1: Wellness & Prevention of Co-Morbidities)*

Moderate to severe cases may require treatment with anti-depressive medications most commonly with newer serotonin reuptake inhibitors (SSRIs) with fewer side effects.

- **Begin Escitalopram 10mgs OD for 2-4 weeks**
  Increase dose to 20 mgs PO OD - if required
  Alternatives include: Sertraline (Zoloft) 50-100 mgs or Fluoxetine (Prozac) 20 mg PO OD

- Advise patients that antidepressant medication should not be stopped without medical supervision.
- If self-stigma is identified, encourage PLHIV to identify supportive family members or friends to assist with counseling and issues regarding disclosure.

- Monitor cases of suicidality and self-harm closely and refer to a higher level of psychological care whenever available.

7.10 HIV & Aging

More than thirty percent of people taking antiretroviral therapy in Botswana are over the age of 60 years, and this number continues to increase annually. While HIV infection speeds up aging processes, the combination of ART and old age also leads to increased multi-morbidity, worsened by the occurrence of geriatric syndromes. These include, but are not limited to, increased incidence of cardiovascular diseases, osteoporosis, metabolic disorders, cognitive impairment, and frailty.

7.10.1 HIV & Aging Health Issues

Medical issues include:
- Late diagnosis of HIV
- **Polypharmacy**
- **Multi-morbidity**
- Geriatric syndromes

Psychosocial issues include:
- **Mental Health**
- Stigma & Self-Stigma
- Loneliness
- Lack of social support systems

7.10.2 Addressing Polypharmacy

Polypharmacy is defined as the simultaneous use of five or more medications by a patient. Use of multiple medications is commonly associated with:
- Poor adherence to medications and increased pill fatigue
- Increased risk of adverse drug events
- Increased possible drug-drug and drug-disease interactions.

More practically, polypharmacy is characterized by some of the following features:
- Prescribing medications that are inappropriate for the patient's medical condition.
- The use of medications that cause adverse drug events and have more drug-drug interactions.
- Underutilization of nonpharmacological measures.
- Prescribing medications that are not necessary for the patient.

To address issues of polypharmacy HIV clinicians should do the following:
- Review medication lists at every visit, including prescriptions, over-the-counter medications, topicals, vitamins and herbal medications. The review should include the following:
  - Rule out drug-drug interactions.
  - Discontinue unnecessary medications and adjust medication dosing as needed.

- Simplify regimens whenever possible.
- Review for the development of any symptoms of adverse side effects.

- In lieu of adding additional medications - Consider non-pharmaceutical approaches (e.g., Sleep hygiene, well balanced diet, physical activity, avoidance of caffeine or alcohol, etc..).

7.10.3 Addressing Frailty

Frailty is characterized by decline in physiologic reserve and increase in vulnerability to adverse life situations, leading to falls, delayed recovery from illness and functional abilities, hospitalizations with worse outcomes and increased mortality.

Frailty is diagnosed by the presence of **at least three** of the following components:

- Unintentional Weight loss
- Self-Reported Exhaustion
- Weakness
- Physical Slowness
- Cognitive Decline
- Low physical activity

Although there are no specific treatments for frailty, frail patients can be optimized with both counseling and pharmacotherapy, using the following interdisciplinary approach:

- Screen patients ≥60 years of age, every 1-2 years if frail or prefrail, less frequently in those who are more robust.
- Address modifiable factors (i.e., smoking cessation, substance use counseling, physical activity, improved diet, etc.)
- Complete a comprehensive geriatric assessment, which includes:
  - Management of any polypharmacy
  - Regular medication review

CHAPTER 8
ART Failure Management

With the introduction of second-generation integrase inhibitors, very rarely will an ART naïve patient develop ART failure leading to the development of HIV drug resistance (HIV-DR). Still, **HIV-DR can develop** and so at the first detection of an elevated viral load clinicians must take action to determine the causes and immediately rectify the situation.

Monitor viral loads closely to detect out-of-range results (VL › 200 copies/ mL) as soon as possible.

- All clinics must develop and implement effective and sustainable procedures for reviewing laboratory reports **within 48 hours and take action** on all detectable viral loads as well as other abnormal laboratory results.
- All clinics must establish an ongoing Failure Management Team to address treatment failure comprehensively, including adequate psychosocial support.

8.1 Definition of Treatment Failure:

- Viral load › 200 copies/mL, 6 months after ART initiation (primary failure).
- Detectable viral load, after documented virologic suppression to ‹200 copies/mL and confirmed by an additional priority viral load (PVL) that is equal or one log higher than the first out-of-range measurement.

It is important to note that children, adolescents and adults who start ART with very high viral loads (› 750,000 copies/mL) may take more than 6 months to reach full viral suppression. Once non-resistance causes of treatment failure are addressed:

- If patients continue to drop at least 1 log with every viral load measurement – do not change their treatment regimen but continue to monitor every 4-6 weeks until full Viral Load Suppression (VLS) is achieved.
- Continue to monitor children and adolescents every 4 weeks.
- When in doubt, discuss such cases with an adult or pediatric HIV specialist.

8. 2 Definition of Immunologic Failure:

- Immunologic failure (CD4 ‹200 cells/µL after more than 1 year on ART) with full VLS.

It is important to note the following:

- **Although some of these patients may never reach CD4 levels above 200, DO NOT change treatment regimens.**
- Diligently screen for OIs and cancer at every clinical visit.
- Screen **annually** for cervical cancer in women, when clinically indicated.
- Prophylactically treat with CTX until CD4 counts have remained above 200 for 6 months for those who have been treated for TB or cryptococcal meningitis *(see Section 7.3.2 for further information).*

These scenarios often occur in patients who had been infected with HIV for a long time before initiating ART. It is also important to note, that despite their lower CD4 count, many of the patients remain clinically stable for many years. Discuss with an HIV specialist as required.

8.3 Management of ART Treatment Failure

At the first detection of an out-of-range viral load, contact the patient and ask them to return to the ART facility to:

1. Identify all possible causes of failure:

- Non-adherence – this will be the likely cause of elevated viral loads in integrase treatment naïve patients.
- Development of OIs, TB, Cancers, COVID-19 or other clinical conditions.
- Incorrect dosage of ART.
- GI disturbance and malabsorption.
- **Adverse reactions to ART such as: rash, insomnia, headache, nausea.**
- Adverse drug-drug interactions such as: Rifampicin with PIs or Doravirine use and/or use of traditional medicines and/or cations with DTG,
- Depression, substance abuse or other psychosocial issues.
- Self-stigma and disclosure issues particularly in adolescents.

2. Address all possible causes of treatment failure:

- Intensify adherence interventions with adequate counselling.
- Provide referrals to appropriate clinical, social work or mental health services (including substance abuse support groups).
- Correct dosages and address any adverse drug-drug interactions.
- Treat all clinical causes (i.e., gastroenteritis).
- Encourage disclosure to at least one supportive friend, family member or peer.

3. After identifying and correcting possible causes of treatment failure:

- **Ask the patient to return to the clinic laboratory in 4-6 weeks to complete a PVL and schedule the clinical follow up** with an adherence partner 2 weeks after the confirmatory PVL is taken. Then proceed with the instruction as outlined in Table 24 below.

Table 24: Management of Out-of-Range-VLs

Step	If Viral Load Measurement is:	Action
1	If confirmatory VL is ≤200 copies/mL	- Maintain current ART regimen and repeat PVL in 3 months. - If suppressed at 3 months return to 6-month clinical follow up and VL testing.
2	If VL has dropped **at least** 1 log less than the first out-of-range viral load	- Continue the current ART regimen and ask the patient to return in 4-6 weeks for another PVL and schedule follow up in 2 weeks. - When PVL results return then follow Steps 1-4 as required.
3	If VL has NOT dropped by at least 1 log	- Begin **Directly Observed Therapy (DOT) for 30 days.** - Send a PVL on Day 30. - Schedule clinical follow up in 2 weeks. - When VL results return repeat Steps 1 – 3 as required.

	Action After Completing DOT for 30 Days	
4	If VL is <200 copies/mL	- Stop DOT. - Maintain current ART regimen and repeat PVL in 3 months. - If suppressed at 3 months return to 6-month clinical follow up and VL testing.
5	If VL is >200 copies/mL	- Stop DOT. - **Send Resistance Test.** - Ask the patient to return in 4 weeks for results.

Resistance Testing (RT)

Send RT regardless of treatment line. All RT results must be tracked, followed up and discussed with an HIV Specialist. Particular attention must be given to:

- All confirmed failures on DTG, DRV/r and/or DOR based regimens.
- Patients with complicated treatment histories and/or highly treatment experienced failures.

Note:

- No RT should be requested before DOT has been completed.
- After DOT subsequent VLS confirms adherence issues.
- Viral amplification is more successful when VL >1,000 copies/mL. However, there are exceptions. Following DOT when viral loads have stopped treading downwards by at least 1 log and remain between 400 – 1,000 copies/ mL - send specimens for RT.
- **Call the NHL and an HIV Specialist - if RT results are not returned within one month.**
- Always send RT for patients on DTG, DAR/r or DOR regimens.
- Clearly document on RT requisition forms (and within the patient's medical records) ART treatment histories and whether patients were INSTI Naïve or INSTI experienced at the time of resistance testing.

When VLs results are NOT available consider the possibility of ART failure when:

- Patients develop of an opportunistic infection or other serious clinical event.
- A significant decrease of CD4 count occurs.
- An abnormally high CD4 count occurs (i.e., >1,000 cells/µL).

In cases when lab monitoring is challenged and the PVL result are not returned within 2 weeks (especially when there is clinical deterioration) contact the NHL and an HIV specialist for assistance.

8.4 Implementation of Directory Observed Therapy (DOT)

- Determine whether it is feasible for the patient to come to a health facility from Monday through Friday to have their doses of ART supervised.
- Advise patients and their adherence partners that doses given on Saturday and Sunday should be supervised at home.
- In cases when facility-based DOT is NOT feasible, provide the client with a 30-day calendar so that a family member can document supervised DOT at home.
- **Be sure to clearly document patient's contact details for tracking.**

8.5 Indications for Priority Viral Loads

- All patients under 20 years of age.
- Confirmatory VLs to determine virological failure.
- Before switching or substituting 1 or more medications (if not already completed within the last three months).
- The follow up VL after treatment switch or adjustments made for poor adherence, drug-drug interactions, adverse side effects or severe GI disturbance.
- All pregnant women.

Always Remember to:

- clearly label "**PRIORITY VL**" on lab requisition forms, including patient file numbers.
- clearly document patient's current cell phone numbers in their manual/medical files for tracking purposes.

8.6 Indications for Consultation with HIV Specialist:

- Failure to achieve VL suppression (‹200 cells/µL) in a pediatric or adult patient after 6 months on ART and who have completed DOT.
- Infants whose DNA-PCR results are pending and clinically unstable.
- ART initiation of infants ‹1 month of age.
- Interpretation of genotypic resistance testing.
- Designing 2nd and 3rd line regimens after resistance testing.
- Difficult decisions regarding the use of PEP or PrEP.
- Difficult decisions regarding ART optimization or regimen switching (and whenever in doubt).
- Special order approval for ART or other medications.

(See Annex 2: HIV Specialist Directory)

CHAPTER 9
Prevention & Management of OIs & Co-Morbidities

9.1 Wellness and Prevention of Co-Morbidities

Botswana is now recognized as having one the largest aging HIV cohorts globally. Therefore, the sustainability of the National HIV Response depends not only on achieving targets for HIV prevention, testing and access to ART, but also and most importantly, with keeping PLHIV healthy and free of co-morbidities. However, regardless of age, PLHIV should be encouraged and properly instructed on the importance of lifestyle changes that will improve their health and quality of life. Concerns about possible weight gain associated with ART should also prompt clinicians to monitor weight gain closely and routinely discuss the importance of healthy lifestyle modifications.

Promoting Wellness begins with healthcare workers providing their patients with information on the Six Pillars of Wellbeing *(according to the Association of Lifestyle Medicine)* that include:

- **Improving Nutrition**
  - Recommend increasing whole plant and grains into diets and decreasing unhealthy fats, processed foods and excess carbohydrates and sugars.
  - Increasing vegetables high in fiber (i.e., morogo and other green leafy vegetables, cabbage, carrots, butternut squash, beet root, beans, etc.)
  - When necessary, refer patients to dieticians and/or include other family members in discussions.
- **Increasing Physical Activity**
  - Recommend exercise regimens, such as walking 3-4 times per week for 30-40 minutes, going to the gym, gardening, dancing and yoga, etc.
- **Decreasing the Use of Recreational Drugs & Alcohol**
  - Always screen for alcohol abuse and addiction and refer patients to community services that address these issues such as local meetings of Alcoholics Anonymous (AA) and Narcotics Anonymous (NA) and if necessary, referral to district psychological services, Sbrana Psychiatric Hospital in Lobatse *(phone: 530-5535)* or other inpatient facilities.
- **Improving Restorative Sleep**
  - Ask patients about the quality of their sleep and make recommendations to improve their sleeping habits. These include decreasing computer screen time in the evenings, disconnecting social media apps at night, refraining from consuming foods or drinks containing caffeine after 4pm.
- **Identifying and Reducing Stressors**
  - Always screen patients, particularly those with clinical or mental health challenges for modifiable psychosocial issues (these include toxic relationships, excessive debt, and other addictive behaviors).
  - Refer to social work in cases that require additional or targeted interventions.
- **Encouraging Social Connections & Community Involvement**
  - Assess levels of stigma and discrimination (both self-inflicted and experienced) and encourage disclosure to trusted friends and family.
  - Encourage participation in community support groups and non-judgmental spiritual congregations that support PLHIV, whenever necessary.

9.2 Prevention of Tuberculous

TB Preventative Therapy (TPT) for PLHIV was re-instituted in 2019, following the commitments made at the UN High Level Meeting on TB in New York in 2018, in which countries including Botswana committed to the ambitious and powerful political declaration to accelerate progress towards the End TB. To improve TPT completion rates and reduce the associated side effects of prolonged isoniazid use, Botswana has implemented the use of once weekly isoniazid combined with rifapentine, known as 3HP.

9.2.1 TPT Eligibility & Considerations

- Adult and adolescent PLHIV who have a negative TB symptom screen.
- Asymptomatic children that are contacts of bacteriologically confirmed TB cases:
  - Less than 5 years old, irrespective of HIV status (INH only)
  - 6-12 years old if HIV positive (INH only)

Before initiating TPT, counsel patients regarding its risks and benefits. Be certain that adult and adolescent patients understand that all 12 doses of 3HP must be taken to complete a full course and optimally prevent active TB.

TPT is designed only for the treatment of latent TB infection.
Patients with active TB symptoms or diagnosis require a full course of ATT.

- Identify eligible clients by using the TB screening algorithm listed on Table 25, below.
- The use of chest Xray is not required, unless clinically indicated.

Table 25 : Eligibility & Contraindications to TPT (3HP or 6H)

ELIGIBLE FOR 3HP/INH	NOT ELIGIBLE FOR 3HP/INH
PLHIV › 12 years of age who have been clinically stable on ART for a least 6 months.	Anyone with symptoms of active TB: cough, fever, weight loss, night sweats and/or: ▪ HIV viremia (›200 copies/mL) ▪ CD4 ‹200 cell/ µL ▪ Clinical evidence of hepatitis ▪ Elevated LFTs ▪ Acute or chronic liver disease ▪ Moderate or heavy alcohol use ▪ Pregnancy and up to 2-3 months post-partum ▪ Previous reaction to the use of TPT drugs ▪ GeneXpert and/or TB culture positive *Take caution in severely immunodeficient HIV patients who may test negative.* ▪ Previous completion of TPT ▪ Taking ART regimens containing ATA/r, DOR or DAR
Former TB patients who completed treatment more than 2 years ago.	
GeneXpert and TB Culture negative	
<u>REGARDLESS OF HIV STATUS</u>: Asymptomatic children ‹5 years - old who are a contact of a confirmed bacteriological TB case. <u>HIV POSITIVE</u> Children ›5 & ‹12 years old, who are a contact of a confirmed bacteriological TB case (INH)	

Emphasize the following educational points when counselling patients on the use of TPT as outlined in Table 26 below. *(For further information see Annex 6: Difference between Latent and Active TB).*

Table 26: Educational Points for Initiation of TPT

TPT	TB
Risk and benefits of TPT	Difference between LTBI and Active TB
Importance of adherence and follow-up	What is TB? How does it spread? What are the signs /symptoms?
Potential side effects of 3HP/INH and what to do if they occur	Relationship between TB & HIV
Duration of treatment	How ART can reduce the risk of TB

9.2.2 TPT Regimens

When to Initiate TPT: 6 Months after ART initiation in clinically stable PLHIV.

3HP: Once-weekly Isoniazid (INH) plus Rifapentine (RPT) Regimen for twelve weeks.

Considerations:

- The regimen will be self-administered.
- There is no need for dose adjustment of DTG.
- PLHIV older than 12 years of age.
- **PLHIV whose viral load is >200 copies/ µL should not be initiated on 3HP until they achieve full VLS.**

9.2.3 Laboratory Monitoring of TPT

Always document normal LFTs at the 6-month post ART visit before 3HP initiation then at 1-month and 3-month post 3HP initiation.

Table 27: 3HP Laboratory Monitoring Schedule

Baseline visit	3-month visit	ART 6-month visit		ART 12-month visit	ART 12-month visit
Initiate ART	LFTs	**Initiate 3HP LFTs**	TPT 1-month visit AST, ALT	TPT 3-month visit AST, ALT	AST, ALT

9.2.4 Breastfeeding Women

3HP should not be administered during pregnancy and breastfeeding. Once breastfeeding is complete women may then initiate 3HP.

9.2.5 Infants & Children

Because of their age, infants and young children who have been in contact with confirmed TB cases are at high risk for progressing to more severe forms of TB disease if infected. The risk of INH-related hepatitis in infants and children is minimal.

- **Asymptomatic Children:**
  - Ages 2-5 years, who are contacts of a bacteriologically confirmed TB case should receive INH for 6 months - **irrespective of HIV status.**

- HIV positive children aged 2-12 years who are contacts of a bacteriologically confirmed TB case should receive INH for 6 months.

Always exclude TB disease by comprehensive symptom screening before initiating TPT

9.2.6 Managing TPT Adverse Events

3HP is generally effective, safe, and has higher completion rates and lower rates of hepatotoxicity than the longer 6 months regimen with INH monotherapy. To ensure safe and efficacious treatment, assess all TPT patients at the end of month 1 and month 3 for adherence, LFTs and any other adverse events.
(see Table 27 above).

Table 28: TPT Monitoring Adverse Events

Medication	Possible Adverse Event	Management
INH	**Elevated AST/ALT**: Asymptomatic elevation of LFTs occur in 10%–20% of people taking INH.	› Closely monitor LFTs › Exercise caution at any LFTs elevation & monitor monthly to ensure a downward trend. › Stop INH if 3x the upper limit of normal LFTs and associated with symptoms.
INH	**Drug induced hepatitis**: Drug induced hepatitis occurs in less than 1% of people taking INH and is more common when INH is combined with other hepatotoxic agents. Factors that may increase the severity include daily alcohol consumption, underlying liver disease or risks for liver disease, such as the concurrent use of medications that are metabolized in the liver.	Stop TPT › If LFTs are 3x the upper limit of normal and patient is symptomatic also stop TPT and monitor weekly. › If LFT are 5x the upper limit of normal also stop ART › Monitor closely and ensure that LFTs have normalized – then reinitiate ART. › Consult an HIV Specialist as necessary.
INH	**Peripheral Neuropathy:** Occurs with INH use more frequently in PLHIV than the general population at normal doses. Risk factors include: diabetes, alcoholism, malnutrition, B12 deficiency, CKD, other medications and being elderly.	› Prescribe pyridoxine (B-6) at 50 mg/daily to those with risk factors. › May increase dosage to 100 mg/daily in refractory cases. › Monitor closely. › If PN persists after two weeks, stop TPT but continue ART.
Rifapentine (RPT)	**Hepatoxicity:** Occurs less frequently with 3HP than 6 months of INH.	› **Follow algorithm as outlined above for INH.**
	Flu-like syndrome: fever, muscle aches and weakness.	› Stop 3HP
	Hypersensitivity Rxns: hypotension, anaphylaxis, nephritis, thrombocytopenia. Can also include fever, headache, dizziness, musculoskeletal pain, petechiae and pruritis.	
	Gastrointestinal Symptoms: nausea, anorexia, severe pain	
	Discoloration of body fluids: Orange-red bodily fluids (i.e., urine, breastmilk). Usually harmless and reverses after	› **Continue 3HP** › **Education PLHIV that there is no need for alarm.**

	treatment.	
Monitor patients with underlying risk factors for liver disease monthly		
If PLHIV present with nausea, vomiting, abdominal cramps, jaundice, persistent fatigue or weakness, unexplained anorexia or dark urine (not just yellow discolored): › Hold TPT › Obtain LFTs and monitor closely IF ALT is ›3 times ULN monitor closely send LFTs weekly. Stop ART if LFTs continue to trend upward not higher than 5x ULN.		
Immediately report any TPT associated adverse events leading to admission or death to BOMRA and the MoH ART Department		

9.2.7 Classification of TPT Outcomes:

Table 29: TPT Outcome Classification

TPT Outcome	Definitions
Completed	Completed 12 weeks of medication within 16 weeks.
Stopped	Treatment stopped by clinician for adverse event or any other reason (remember to document the reason on the medical records and forward information to BOMRA) Treatment stopped by patient, document reasons in the medical record.
Active TB	Developed TB disease while on TPT – immediately send specimen for GeneXpert TB culture.
Lost to follow-up	Did not complete the 12 doses in 16 weeks.
Died	Died while taking TPT.

9.3 Hypertension & Cardiovascular Disease

Management of hypertension (HTN) is essential to prevent further development of cardiovascular disease (CVD). As the number of PLHIV who have been on ART for many years increases, complications from HTN, CVD and metabolic dysfunction also continue to increase. Because these conditions seldom arise in isolation, an integrated approach to control HTN and CVD, which includes weight management, lifestyle modifications and optimized antihypertensive medications are essential.

Determining the 10-year CVD risk category should guide clinical management. Although large scale clinical trials of CVD risk in PLHIV in Sub-Saharan African populations continue, the 10-year CVD risk category, especially for those already diagnosed with HTN or CVD, can be adapted from larger European and American cohort studies. By assessing PLHIV CVD risk, clinicians can educate patients and agree upon the best treatment options to maintain cardiovascular health.

9.3.1 Assessing 10-Year CVD Risk

Document the 10-Year CVD Risk Category as follows *(adapted from the 10-year CV risk categories SCORE system)*

Very High Risk:

- Previous myocardial infarction, stroke, TIA, aortic aneurysm, peripheral artery disease, acute coronary syndrome, coronary or arterial revascularization.
- Diabetes Mellitus with target organ damage (e.g., proteinuria or grade 3 HTN or hypercholesterolemia).
- Severe Chronic Kidney Disease (CKD) (eGFR/CrCL<30).
- Unequivocal CVD on imaging, including >50% stenosis on angiography or ultrasound.

High Risk:

- Elevation of any one of the following:
  - Cholesterol >8 mmol/L
  - Familial hypercholesterolemia
  - Grade 3 HTN (BP≥180/110 mmHg)
- Diabetes Mellitus
- HTN with Left Ventricular Hypertrophy (LVH)
- Moderate CKD (eGFR/CrCL=30-59)

Low to Moderate Risk:

- Grade 2 HTN

9.3.2 Grading & Diagnosis of HTN

Using Table 30, *adapted from the EACS 2021 Guidelines*, determine the level/grade of HTN, as outlined below:

Table 30: Determining Hypertension Levels

Blood Pressure	Primary Action	Drug Treatment	Notes
High Normal BP 130-139/85-89 mmHg	For all levels: Provide Lifestyle Advice & Diet Modification	**High Normal:** Consider drug treatment in very high-risk PLHIV with CVD & CAD	Recheck BP after 3 months.
Grade 1 – HTN BP 140-159/90-99mmHg		**Grade 1:** Immediate drug treatment in high or very high-risk PLHIV with CVD, CKD or HMOD*	**Grade 1:** If no improvement after 3 months of lifestyle modification, begin drug treatment
Grade 2 – HTN BP 160-179/100-109 mmHg		**Grade 2 & 3:** Immediate drug treatment in all persons.	**For all levels:** Aim for BP control within 3 months
Grade 3 – HTN BP>180/110 mmHg			

9.3.3 Treatment of HTN

Apply the following step wise sequencing principles to treat PLHIV with HTN as outlined below.

- Start at the lowest dose of each medication and increase as required before adding more medications.
- To improve adherence, whenever available, use fixed dose combinations to decrease pill burden.

- Commonly available FDC antihypertensives include:
  - **CCB+ARB:** Amlodipine + Telmisartan *(FDC Brand name: Twynsta (Amlodipine 5mg + Telmisartan 40mg. Also available at increasing doses) or FDC Generic: Amlotel same dosages)*
  - **Thiazide + ARB:** HCTZ + Telmisartan *(FDC brand name: Co-micardis: 40/12.5mg also available in 80/12.5mg, also available at increasing doses)*
  - **ACEi + CCB:** Enalapril (5/10/20mg + Amlodipine 5/10mg)

- Treat HTN as follows:

STEP ONE – Dual Therapy

- [ACEi *(e.g., Enlapril 20mg OD)* **or** ARB (*e.g., Telmisartan 80 mg OD*]
  plus CCB *(e.g., Amlopidine 5-10mg OD)* **or** *if available an alternative to HCTZ (e.g., Indapamide 2.5 mg OD)*
  Always use FDC when available (see above)
- **Monotherapy** can be considered *rather than dual therapy* in low-risk Grade 1 HTN (systolic BP<150) or in the older and fragile patients *(preferable ACEi or ARB, avoid HCTZ monotherapy)*.

STEP TWO – Triple Therapy

- **Add** (ACEi or ARB) + CCB + Thiazide-like diuretic,
  whichever medicatiosn that has not been used in dual therapy.

STEP THREE – Triple Therapy + Alpha or Beta Blocker

For Resistant Hypertension, add as required:

- Spironolactone (25-50 mg OD) or
- Alpha-blocker (Doxazosin, 4-8 mg OD)
- Beta-blocker (Carvedilol 25 mg OD or BD or Bisoprolol 5-10 mg OD)
- **If BP remains elevated after maximum doses – refer for a cardiology consult.**

Remember: Start at the lowest dose of each medication and increase as required before adding more medications.

Also consider the following:

- If amlodipine is not available substitute with Nifedipine.
- Do not begin with Beta-blockers except in the following:
  - Heart failure, angina, post MI, atrial fibrillation or younger women planning pregnancy and resistant hypertension.

- *Although not yet available in the public sector, the combination of Indapamide + Amlodipine + perindopril is available and can be used in the private sector as an FDC (1 pill daily).*
- While most first-line ART regimens do not interact with most antihypertensive medications, interactions with the use of PIs are more common. *(Refer to Table 31 below for a listing of expected DDIs of ART & HTN medications.)*

(The table below was adapted from EACS European AIDS Clinical Society, Guidelines 11.0, PART IV & European Society of Cardiology Guidelines 2018, European Heart Journal (2018) 39, 3021-3104 doi:10.1093/eurheart/ehy339 and the American Diabetes Association Standard of Care 2023)

Table 31: DDI with ART and HTN medications

Medication	ATA/r	DRV/r	DOR	ETV	RPV	CAB oral	CAB/ RPV	DTG	TAF-ED	TLD	TRU
captopril											
enalapril											
perindopril											
ramipril											
candesartan											
losartan											
telmisartan											
valsartan											
atenolol											
bisoprolol											
carvedilol											
labetalol											
metoprolol											
propranolol											
amlodipine											
diltiazem											
nifedipine											
verapamil											
amiloride											
furosemide											
hydrochloro-thiazide											
indapamide											
doxazosin											
hydralazine											
methyldopa											
prazosin											
sacubitril											
spironolactone											

Legend: **Green:** No clinically significant interaction expected
Yellow: Potentially weak interaction, adjustments less likely required
Orange: Potential significant interaction, requires close monitoring, alternative dosing and/or adjustments in timing.

9.3.4 Special Consideration: HTN & Diabetes

The American Diabetes Association Standard of Care for 2023, now recommends lower BP targets for people with HTN and DM at 130/80 (or less) with LDL below 1.8 mmol/L and no greater than 1.42 mmol/L, depending on CVD risk. Observe these targets when prescribing medications for HTN and DM in PLHIV.

9.3.5 Treatment of Dyslipidemia

Beginning in 2023, screen all PLHIV ›50 years, annually for dyslipidemia. Treatment with lifestyle modifications (improved diet, exercise, smoking cessation and alcohol reduction) and the use of statins are first line interventions.

- Treat mild elevations with lifestyle modifications and monitor closely. If inadequate response within 3 months, begin at the lowest dose and titrate the following:
  - **Atorvastatin 10-80mg PO OD**
  - **Rosuvastatin 5-40mg PO OD (**available in the private sector)
  - **Simvastatin 10-40mg PO OD**
    - Contraindicated with protease inhibitors.
    - Use lower doses with NNRTIs

Note: **Pitavastatin** has been successfully used in clinical trials including in Botswana and has confirmed anti-inflammatory effects. When it becomes available, recommendations for its use will be made.

Table 32: Treatment Targets for High and Very High CVD Risk

10 Year CVD Risk *(refer to section 9.3.1)*	Reduce to LDL Target Level
High	1.8 mmol/L
Very High	1.4 mmol/L

9.3.5a Elevated Triglycerides:

It is critically important that clinicians understand that the presence of hyperglyceridemia can be due to poorly controlled diabetes.

- Annually monitor lipid and glucose for all patients
- Educate patients about the important of decreasing their sugar & carbohydrate intake.
- If not already on statins, begin treatment when TG›2.3 mmol/L
- Triglyceride levels ›10 mmol/L greatly increase the risk of pancreatitis.
  - Treat triglycerides ›10 mmol/L: with Bezafibrate 400 mg PO OD

9.4 Management of Kidney Disease

The spectrum of HIV-associated renal diseases includes diseases:

- Directly associated with infection
- Linked to the systemic immune response to infection.
- Developed as a consequence of super-infections.
- Associated with the treatment of HIV infection.

Negative prognostic factors for Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD) in HIV includes Black race, low CD4 counts, high viral loads, older age, the presence of HTN, T2DM and CVD. Therefore, all patients on ART must have eGFR/CrCl routinely monitored. This is particularly critical for patients who have already been identified with risk factor for CKD.

- Initiate all patients with evidence of CKD on triple ART (TAF-ED) as soon as possible and monitor closely for improvement of renal function tests (RFTs).

- Do not initiate DAR/r with TRU if eGFR/CrCl is ‹70 ml/min as the tenofovir level is increased and can further increase renal toxicity.

- Follow the instruction in Table 32 below, for 3TC dose reductions with CKD on triple therapies. Take note that there is no longer need to administer 3TC as a liquid formulation to adults.
- Do not use TAF-ED if eGFR/CrCL is ‹50 mls/min., instead discuss individual cases directly with an HIV Specialist to determine appropriate dose reductions.

Table 33: Dose Reduction of 3TC in ABC containing regimens

eGFR/CrCL	3TC Dose
›50 mL/min	300 mg PO OD
30-49 mL/min	150 mg PO OD
‹30 mL/min	150 mg PO Three times/week
Hemodialysis	300 mg PO Q weekly

Beginning in 2023, all virologically suppressed patients on TAF-ED or ABC containing regimens will be switched to dual therapy: 3TC + DTG to prevent further kidney function deterioration and long-term ART toxicities. Routinely monitor renal function, *as recommended in Section 6.4.*

Discuss patients who are not virally suppressed on TAF-ED or ABC containing with an HIV specialist to determine eligibility for other dual therapy combinations.

Work up for CKD should include:

- Determination of any renal risk factors
- Discontinuation or adjustment of any nephrotoxic medications (including TDF and/or TAF)
- Completion of renal ultrasound
- Referral to Nephrology if there is:
  - Unexplained AKI or CKD
  - No improvement and/or progressive reduction of eGFR/CrCl
  - Presence of hematuria or proteinuria
  - Advanced CKD (eGFR/CrCL ‹30 mL/min.)
- If hypertensive with proteinuria, ensure that an ACEi or ARB is being prescribed.
- If urine dipsticks are not available send urine for urinalysis and albumin/creatinine ratio.

Whenever possible measure eGFR/CrCL automatically using appropriate apps. *(See: National Kidney Foundation app available for iPhone, Android and iPad, on Google Play and the Apple Store).*

9.5 Management of Bone Demineralization

Aging is the most common risk factor for the development of osteopenia and osteoporosis. Long-term exposure to TDF containing regimens and post-menopausal women exacerbates bone demineralization. Suspected cases can be confirmed with DexaScan, when available.

Empiric Treatment may include daily Calcium and Vitamin D supplementation.

9.6 Diagnosis & Management of Metabolic Syndrome

As PLHIV age and/or have been exposed to previously toxic ART regimens and/or medications for co-morbidities, their risk for development of Metabolic Syndrome increases. The condition presents as a cluster of disorders, which drastically increase the risk of developing CVD (particularly heart failure and stroke).

Diagnosis can be made when the following cluster of conditions occur:

- Hypertension
- Elevated Triglycerides & Cholesterol (low HDL, high LDL)
- Insulin Resistance &. Type 2 Diabetes
- Lipodystrophy (including increasing waist circumference)
- Obesity
- High waist to hip ratio

Promptly identify metabolic syndrome and aggressively manage each clinical condition with lifestyle modifications *(diet, exercise, alcohol and tobacco cessation)* and medications as required to prevent further progression and onset of more serious pathology.

Carefully monitor all patients who have been on ART regimens for ›10 years, are over 50 year of age and particularly those that received:

- DDI, D4T
- CBV/NVP or EFV
- Protease Inhibitors

9.7 Prevention & Management of Type 2 DM

It is estimated that 6% of the general population in Botswana suffers from Type 2 Diabetes and many go undiagnosed. Annually monitoring random blood glucose will ensure that T2DM in PLHIV are promptly diagnosed and optimally treated.

9.7.1 Screening & Diagnosis

- Send random glucose for all newly initiating patients and annually thereafter.
- Follow the stepwise algorithm outlined in Table 33 below, to establish the diagnosis of Pre-Diabetes and T2DM.

Table 34: Screening & Diagnosis of T2DM

Test	Result	Next Step	Diagnosis	Action
Random Glucose	‹6 mmol/L	Reassurance	→	Screen Annually
	› 6 mmol/L	Fasting Glucose		
	› 11.1 = high suspicion T2DM	Confirm with GTT* or HbgA1C		
Fasting Glucose	Between 6.1 and 6.9 mmol/L	→	Impaired Fasting Glucose	Lifestyle intervention repeat FG in 3 months.
	Between 7.0 – 11.00 mmol/L,	Confirm T2DM with either GTT or HgbA1c.		
*Glucose Tolerance Test (GTT)	GTT of ›11.1 at 2 hours	→	T2DM	Lifestyle intervention and medication (if HgA1C is 7%)
HbgA1C	6.0 – 6.4% Pre-diabetes	→	Pre-Diabetes	Lifestyle intervention repeat in 6 months.
	› 6.5%	→	T2DM	Lifestyle intervention and medication (if HgA1C is 7%)

- Educate ALL patients suspected of T2DM of lifestyle modifications regardless of their diagnosis.

- **Pre-Diabetes** should be considered in the following:
  - Impaired Fasting Glucose
  - Impaired glucose tolerance
  - HgbA1C between 6.0-6.4%
  - Gestational diabetes
  - Steroid induced diabetes
  - Previous COVID-19 infection with elevated glucose

9.7.2 Treatment of T2DM

Treat PLHIV confirmed with T2DM requiring medications as follows:

- Prescribe Metformin 500mg PO BD
  (maximum dosage for DTG based regimens is 1,000mg OD)
- Educate all patients on the importance of lifestyle and diet modification.
- PLHIV at high risk for CVD, already established heart failure or CKD may benefit from additional DM medications that are available.
- Refer PLHIV with severe renal dysfunction (eGFR/CrCl <30) to a local DM clinic if available in their location for further management of DM medications. If a DM clinic is not available, refer to medicine clinics.
- Monitor glucose at routine HIV visits when poor control is suspected.
- Discuss with an HIV Specialist or Diabetes Specialist, as needed.

9.8 Management of Sexually Transmitted Diseases

The diagnosis of sexually transmitted diseases is a seminal event that requires a comprehensive clinical work up in view of the high risk of dual and multiple co-infections. This includes HIV testing, partner tracing and individual and/or syndromic treatment. In addition to the following:

- It is essential to take a nonjudgmental approach that is respectful and compassionate at every patient encounter to overcome stigma and shame.
- Counsel, educate and share information with patients to enable strategies to prevent recurrences and adoption of safer sexual behaviors.
- Adopt a syndromic approach as outlined in Table 35, which has been adapted from *The Management of STIs and Key Populations Competency, September 2022.*

Table 35: STI Syndromes & Recommended Treatment

Description	Disease / Causative Agents
Urethral Discharge Syndrome (UDS) **Most Common Symptoms** ▪ Urethral itching and discharge ▪ Difficult/painful/frequent urination	Gonorrhea / N. gonorrhoeae Chlamydia/ Chlamydia-Trachomatis Trichomonas / Trichomoniasis *Non-gonococcal Urethritis/ M. Genitalium or T. Vaginalis*

<table>
<tr><td>Vaginal Discharge Syndrome (VDS)
▪ Unusual vaginal discharge and/or odor
▪ Vaginal itching
▪ Difficult/painful urination
▪ Pain during sexual intercourse</td><td>Vaginitis /Trichomoniasis, Candidiasis,
Cervicitis / Gonorrhoea, Chlamydia
Anaerobic/aerobic
Bacterial infection
M. Genitalium</td></tr>
<tr><td>Pelvic Inflammatory Disease (PID)
▪ Abnormal vaginal discharge
▪ Spotting between periods
▪ Uterine tenderness on pelvic exam
▪ History of lower abdominal pain
▪ Pain during sexual intercourse
▪ Cervical motion tenderness
▪ Difficult urination /dysuria
▪ Sometimes nausea, fever, vomiting
▪ Exclude ectopic pregnancy and Appendicitis.
▪ A surgical abdomen requires emergency hospital admission*</td><td>Trichomoniasis
Candidiasis,
Bacterial Vaginosis (BV) (not necessarily an STI)
Gonorrhea
Chlamydia
Anaerobic/aerobic
Bacterial infection
M. Genitalium</td></tr>
<tr><td colspan="2">Syndromic Treatment:
Ceftriaxone 250 mg IM stat
Azithromycin 1 g PO stat
Metronidazole 2 g PO stat
Fluconazole 200 mg PO stat

In cases of GC resistance: Treat with Ceftriaxone 500 mg IM stat, submit urine and swab specimens.
If cephalosporin allergy: Gentamicin 240 mg IM single dose
If ceftriaxone is not available: Cefixime 800mg single dose + Azithromycin 2 g PO single dose
<u>In cases of PID:</u>
Azithromycin is given 1 g weekly x 2 weeks
Metronidazole 2 g weekly x 2 weeks
*If no response in 3 days, admit for IV antibiotics</td></tr>
<tr><td>Genital Ulcer Disease
▪ Among the most common STI for both men and women.
▪ Increases the infectiousness of HIV, especially with chancroid or syphilis.
▪ Enlarged regional lymphadenopathy.
▪ Women can present with cervicitis, men with urethritis.
▪ Can be asymptomatic with mild or nonspecific clinical manifestations.
▪ Vesicular or non-vesicular lesions
▪ Genital itching/pain</td><td>Genital Herpes / HSV-1 & HSV-2
Syphilis / T. pallidum
Chancroid /
Lymphogranuloma Venereum (LGV)
Granuloma inguinale / Klebsiella.
Granulomatis
Candida Albicans

Concurrent infection with multiple organisms is common.</td></tr>
<tr><td colspan="2">Syndromic Treatment:
Benzathine penicillin 2.4 IU UM stat
Ceftriaxone 250 mg IM stat
Acyclovir 400-800 mg TID x 7 -10 days (may continue for another 7 days in refractory cases)
<u>If penicillin allergy</u>
use Azithromycin 1g weekly x 3 or doxycycline 100 mg BD x 14 days (Note: do not use doxycycline in pregnancy)</td></tr>
<tr><td>Genital Warts
▪ Common among STI clients
▪ May appear on anus, perianal, penis, vagina, vulva and cervix.
▪ High risk - HPV 16, 18, 31, 33, 35 associated</td><td></td></tr>
</table>

with development of cervical and penile cancers. ▪ HPV 6 & 11, associated with conjunctival, nasal, oral and laryngeal warts. ▪ PLHIV may harbor multiple strains simultaneously, which may be more persistent. ▪ Routine Pap Smear essential for early detection and decreased mortality ▪ HPV quadrivalent vaccine available.	**Human Papilloma Virus (HPV)**
Targeted Treatment: Surgical excision, especially in pre-cancerous and cancerous lesions, which (may also require oncology interventions) Cryotherapy, cauterization for benign and less severe lesions **Topical therapies:** Podophyllin or Trichloroacetic 90% solution, 5 Fluorouracil 5% cream (if CD>200 - Imiquimod apply locally 2-3x per week to lesions) ***In pregnancy use:*** *Trichloroacetic 90% solution*	
Balanitis **Most Common Symptoms** ▪ Inflammation of the glans and prepuce of the penis. ▪ Typically occurs in older men (Zoon's balanitis) and diabetics. ▪ If foreskin is not retractable refer to urology	Candida/Candida Albicans (most common) Poor Hygiene (multiple organisms) Skin Conditions (i.e., Lichen Planus, eczema, psoriasis, dermatitis) Irritants (i.e., perfumes, detergents, etc..)
Syndromic Treatment: **Clotrimazole cream apply locally BD x 7 days** **Metronidazole 2 g state if secondary bacterial infections are present** **Consider Fluconazole 200 mg OD x 3 days** Advise on local hygiene (weak salt solution – avoid soaps) Rule out diabetes (send RBS or glycosuria) Review in 7 days	
Proctitis, Proctocolitis & Enteritis ▪ Usually sexually acquired through oral, genital or digital (hand/finger) contact. ▪ On pathogen confirmation adjust treatment	Gonorrhea / N. gonorrhoeae Chlamydia/ Chlamydia. Trachomatis Lymphogranuloma venereum (LGV)*
Acute Scrotal Swelling (Epididymitis/Orchitis) ▪ Often associated with urethral discharge ▪ Tenderness, swelling, increased warmth of scrotum	Gonorrhea / *N. gonorrhoeae* Chlamydia / *C. trachomatis* Viral infection Pyogenic bacterial infection
Inguinal Bubo ▪ Painful/tender inguinal swelling ▪ If unilateral most likely skin infection ▪ Exclude inguinal hernia.	Chancroid / *Haemophiles ducreyi* Lymphogranuloma Venereum* *Chlamydia /C. trachomatis* Cat Scratch /*Bartonella* *Multiple viral infections (i.e., HIV, hepatitis, mono, syphilis)* Various cancers (lymphoma, KS, leukemia, etc.)
Syndromic Treatment: **Ceftriaxone 500 mg IM x 1 stat** **Doxycycline 100 mg PO BD x 14 days** ***Note:***	

If bloody discharge, perianal or mucosal ulcers, tenesmus and a positive rectal chlamydia test or LGV, extend treatment to 21 days.* ** If both ulcer and bubo, likely LGV add Azithromycin 1 gram PO weekly x 3 weeks*

Neonatal Conjunctivitis ▪ Purulent eye discharge ▪ Swelling of face/eyelids	Gonorrhea / *N. gonorrhoeae* Chlamydia / *C. trachomatis* Pyogenic bacterial infection
Treatment: Ceftriaxone 50 mg/kg body weight, maximum 125 mg, single dose IM Erythromycin 50 mg/kg body weight, QID x 14 days If no improvement after 3 days, send to ophthalmologist	

Table: 36: Additional Information on Individual STI Pathogens
(adapted from : The Management of STIs and Key Populations Competency. September – 2022)

Additional Information on Individual STI Pathogens
Herpes simplex virus ***(HSV-1 & HSV-2)*** ▪ HSV-1 & HSV-2 are lifelong infections, causing painful cold sores (fever blisters) in or around the mouth, or painful ulcers on or around the genitals or anus. ▪ A common virus can be acquired sexually or passed from mother-to-child during birth. ▪ In most people with healthy immune systems, infection is usually latent. ▪ Stress, trauma, menses, other infections, or suppression of the immune system, (such as by HIV), can reactivate the latent virus and symptoms can return. ▪ Recurrence after primary infection occurs in approximately 50% of cases. ▪ Symptoms may include malaise, fever and headache. ▪ In advanced HIV disease, HSV ulcers can become large, deep and mimic chancroid and can affect the bronchus, lungs, esophagus and brain.
Gonorrhea ***(Neisseria gonorrhea)*** ▪ One of the most common STIs. ▪ Affects mucosal surfaces, rectum, pharynx and conjunctivae. ▪ Clinical features include cervicitis, purulent discharge of the penis, proctitis, pharyngitis (usually asymptomatic). ▪ Advanced stages can progress to disseminated gonococcal infection (DGI) causing arthritis-dermatitis syndrome.
Chlamydia ***(Chlamydia trachomatis)*** ▪ Can produce extensive subepithelial inflammation, ulceration and scarring in females & males. ▪ Commonly asymptomatic in males, may cause mucoid, purulent or mucopurulent (most common) penile discharge.
Trichomoniasis ***(T. vaginalis)*** ▪ Pruritic vaginitis and discharge are the most common manifestations
Chancroid ***(Haemophilus ducreyi)*** ▪ Characterized by one or more genital ulcers, with painful inguinal swelling of lymph nodes. ▪ Lesions can be found anywhere on the external genitalia in males and females. ▪ Base of ulcers is usually covered in necrotic, oozing pus and ulcers bleed readily. ▪ Acute suppurative inguinal lymphadenitis develops soon after infection - referred to "bubo" and can develop into abscesses. ▪ PLHIV may require additional treatment in refractory cases.

Syphilis (*Treponema. Pallidum)*

- Progresses if untreated from primary (infectious) to secondary, and early and late latent phases.
- Primary syphilis (usually painless chancre formulation 3-6 weeks post infection)
- Secondary syphilis (2-4 months post infection)
- Tertiary syphilis, 50% if left untreated manifest CVS involvement, neurosyphilis, granulomatous disease, tabes dorsalis, general paresis
- PLHIV may develop neurosyphilis rapidly despite treatment for early syphilis.
- Congenital syphilis can result in still birth, fetal loss, perinatal death, prematurity and low birth weight. Brain and spinal cord involvement can also occur.

Other Skin Infections that can affect the genitalia

- Scabies (treat with permethrine 1% or Ivermectin 200 mcg/Kg body weight PO x 1 dose, repeat in 14 days.
- Lice (pediculosis pubis) (treat with permethrine 1%)
- Molluscum Contagiosum (for PLHIV the treatment is ART)

**For further in-depth information refer to: The Management of STIs and Key Populations Competency. September - 2022*

CHAPTER 10:
HIV Related & Unrelated Cancers

10.1 Cervical Cancer

Approximately 80% of all women will at some point be infected with HPV but most people will clear HPV infection. However, women with weakened immune systems are less likely to clear the HPV virus and become more susceptible to developing pre-invasive lesions that can, if left untreated quickly progress to invasive cancer. In addition, these women are more likely to develop cervical cancer at an earlier age. Due to the high prevalence of HIV in Botswana, contact with women at cervical cancer prevention sites will be used as an opportunity for health education, HIV counselling and testing as well as provision of HIV care. At the same time, cervical cancer screening services must be closely linked to HIV treatment sites and incorporated into routine HIV treatment services.

10.1.1 Primary Prevention

Primary prevention of cervical cancer involves health promotion, education and vaccination of adolescent girls. Primary Prevention efforts should be harmonized with routine vaccination services and other Ministry of Health programs, which implement health promotion and education activities aimed at reducing high-risk sexual behaviour.

HPV vaccines directed against the highest risk HPV types are available worldwide and have the potential to prevent 70-90% of cervical cancers in the future. The subtypes identified among both HIV positive and negative women cover 6, 11, 16, 18 & 45 (2018). A **triage study of HPV positive results with pooled HPV genotypes 16/18/31/33/35/45/52/58 revealed a maintained high sensitivity in detecting CIN2+ among both HIV negative and positive women in Botswana (2021).**

Remember: HPV has increasingly been found to cause oral cancers.
Be vigilant when screening and include oral assessments.

HPV Vaccines are most effective if administered before the onset of sexual activity, that is, before first exposure to HPV infection.

- Administer the recommended HPV vaccines to both females and males from the age of 9 to 13 years. These include:
  - Quadrivalent vaccine (Gardasil, 4vHPV) covers subtypes; 6, 11, 16 and 18.
  - 9– Valent vaccine (Gardasil 9, 9vHPV) covers subtypes; 31, 33, 45, 52 and 58 including the 4 that are covered by the quadrivalent vaccine.
- Administer vaccines intramuscularly on the upper outer aspect of the arm on the following schedule:
  - **HIV Positive:** 3 doses - At 0, 2 and 8 months. (The second dose is given 2 months after the first dose and the third dose 6 months after the second dose).
  - **HIV Negative:** 2 doses - Give the second dose 6-12 months after the first dose.

10.1.2 Secondary Prevention

Due to the high prevalence of HIV in Botswana, cervical cancer screening services must be closely linked to HIV treatment sites and incorporated into routine HIV treatment and care services.

10.1.2a HPV Screening Options:

There are currently three screening options: VIA, Pap smear and HPV DNA testing. Each have variable performance. Priority at a health facility level should be given to providing screening services on the same day that a client seeks other services. Therefore, whichever resource exists in a health facility for screening should be utilized.

- Offer one of the following screening methods listed below to all woman seeking SRH services, as well as women attending postnatal care, in-line with the integrated services plan:
  - **Visual Inspection with acetic acid (VIA)**
    VIA is performed by trained nurses and doctors at designated sites with linkage to treatment services for those who screen positive. The benefit of VIA is that it utilizes a single visit approach where feasible, uses supplies that can be procured locally, and does not rely on laboratory services.
  - **Papanicolaou Smear (Pap Smear)**
    Pap Smear remains the most widely available screening method in Botswana and is provided in all health facilities, including mobile stops. Pap Smear can be performed by all trained health care providers (HCP) including registered nurses (RNs). Pap Smear can be done in women during the postpartum period.
  - **HPV-DNA Testing**
    HPV testing is the international standard for cervical cancer screening and is recommended by WHO where resources allow. The significant benefit of HPV testing in Botswana, is that it does not require a health provider to collect but can simply be collected through a vaginal self-swab. HPV testing also identifies women at an earlier stage of risk and therefore if negative, allows longer spacing between screening intervals. HPV testing can be done in women during the postpartum period. This is positive development in SRH that will go far to save women's lives.

10.1.2b HPV Self-Swab Sample Collection Instructions

Step 1
- Wash your hands
- Twist the cap off the tube and pull out the swab
- Note the red mark on the swab close to the tip

Step 2
- Assume a comfortable position
- Insert the swab into the vagina high up the vaginal canal until you meet resistance
- Push up the swab up to the red mark at the tip

Step 3
- Rotate the swab gently 2-3 times, for about 10 seconds

Step 4
- Remove the swab and place it back in the tube
- Return the tube to the provider

10.1.3 Screening Criteria:

- Women aged 25 to 65 are eligible for cervical cancer screening. In line with the WHO cervical cancer elimination strategy, the National Cervical Cancer Prevention Programme (NCCPP) aims to screen 70% of women by the age of 35 with a high-performance test, and again before age 45.

Screening can be extended to women older than age 65 if they have never been screened or **to women of any age who have had a history of abnormal screening or gynaecological complications.**

Remember: Young women who were born with HIV are likely to present with gynaecological complications at an earlier age.

- Age for VIA eligibility is 25-49 years.
- Women who fall outside of the screening age criteria may be referred for screening with Pap Smear at the discretion of a cervical cancer prevention trained provider.
- Women who are referred for screening outside the inclusion criteria should have a 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.

10.1.4 Action of HPV Results

Negative Results: Repeat screening - regardless of HIV status and regardless of type of screening performed (i.e., Pap, VIA, HPV testing) every 3 years. The exception is for women who are confirmed negative for both HIV and HPV, who should repeat screening every 5 years. However, HIV positive women who present with repeated STI, PID or other gynaecological complications may screen more frequently.

Positive Results: Provide evaluation and treatment according to the Cervical Cancer Algorithms 1-5 below.

10.1.5 Treatment Options & Referrals for Positive Results

To optimize care and reduce mortality, it is essential to link screening with treatment that is safe, effective, acceptable and feasible. The following are the treatment options for women who test positive for an HPV and are identified with minor or large pre-cancer lesions; Cryotherapy, Thermal coagulation and Loop Electro-surgical procedure (LEEP).

- **Cryotherapy**

Cryotherapy is an effective intervention to treat pre-cancerous lesions that can be performed in a clinical setting by a trained nurse without anaesthesia. The National Cervical Cancer Prevention Programme (NCCPP) has successfully scaled-up cryotherapy treatment sites across the country. However, due to challenges of equipment failure, lack of maintenance and inadequate supply of refrigerant gas, further investment in cryotherapy is not planned. Where already available and functioning, however, cryotherapy will still be utilized to treat eligible lesions.

- **Thermocoagulation**

Indications for thermocoagulation are the same as those for cryotherapy and is also performed by trained nurses and doctors, with the advantages of being portable, fast, safe and cost-effective. No anaesthesia is required in the clinical setting and the procedure poses less logistical challenges.

- **LEEP**

LEEP is the optimal treatment option for cervical pre-cancerous lesions seen on VIA that are either large or extend into the endocervical canal or for certain Pap Smear results. LEEP is provided by trained doctors in health facilities under local anaesthesia. LEEP services will be scaled-up to more sites to reduce treatment waiting period to less than one month.

10.1.5a Follow-up & Linkage to Care

A robust system of follow-up is required of women with pre-cancerous lesions to ensure they do not progress to invasive cancer or that if invasive cancer is identified, they are referred for further treatment in a timely manner.

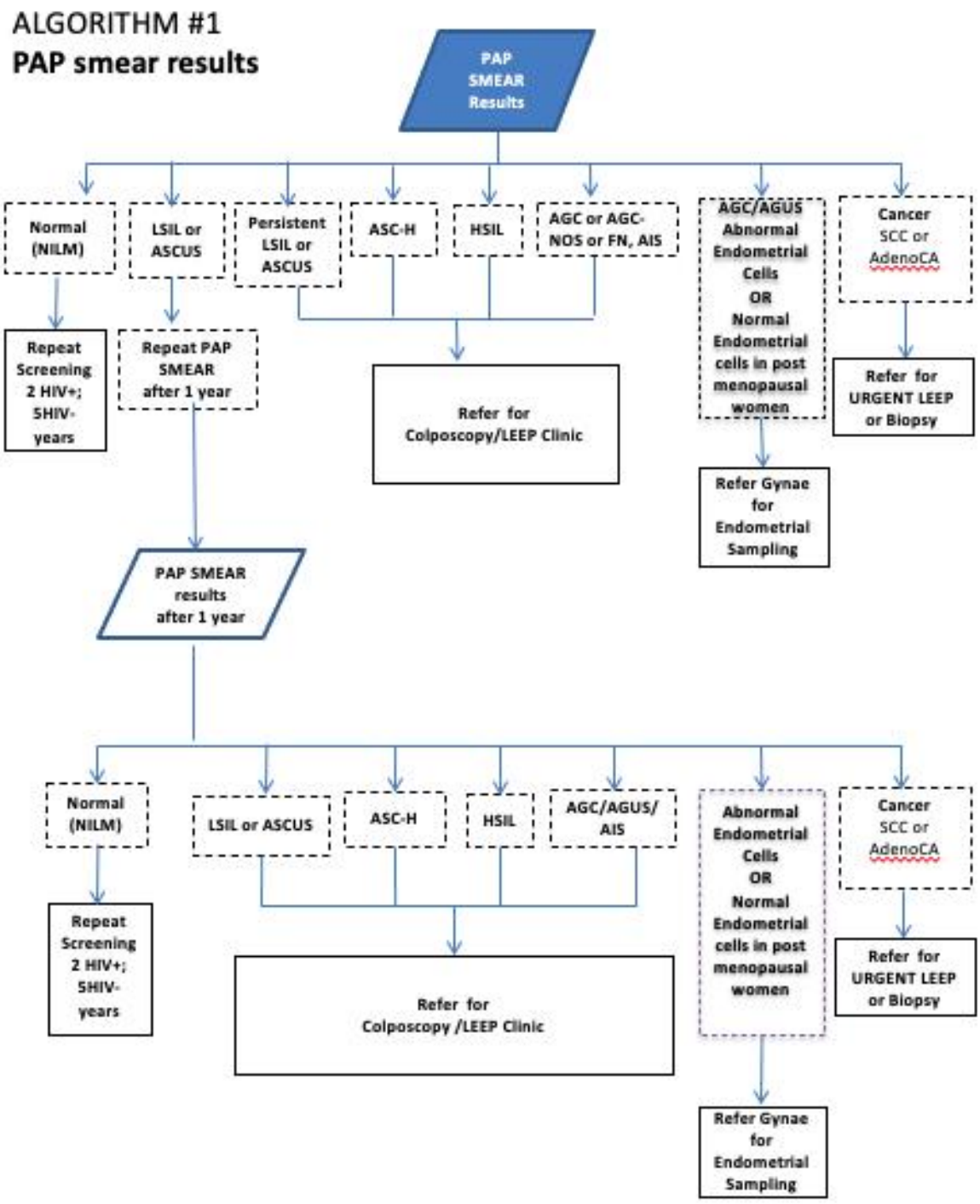
- Give women a review date at the LEEP site within 6 weeks to review their results.
- Give women post-treatment follow-up at 12 months.
    - Call all patients who do not present for their results (within 7 days) for linkage to care if further intervention is warranted.
    - This will include referral from HPV, VIA and Pap screening facilities to LEEP treatment sites, as well as linkages between LEEP centers and gynecology and oncology centers.

Women identified with cervical cancer by clinics and hospitals through patient-initiated visits MUST be linked to care via LEEP clinics or directed to the gynecologic oncology multi-disciplinary clinic.

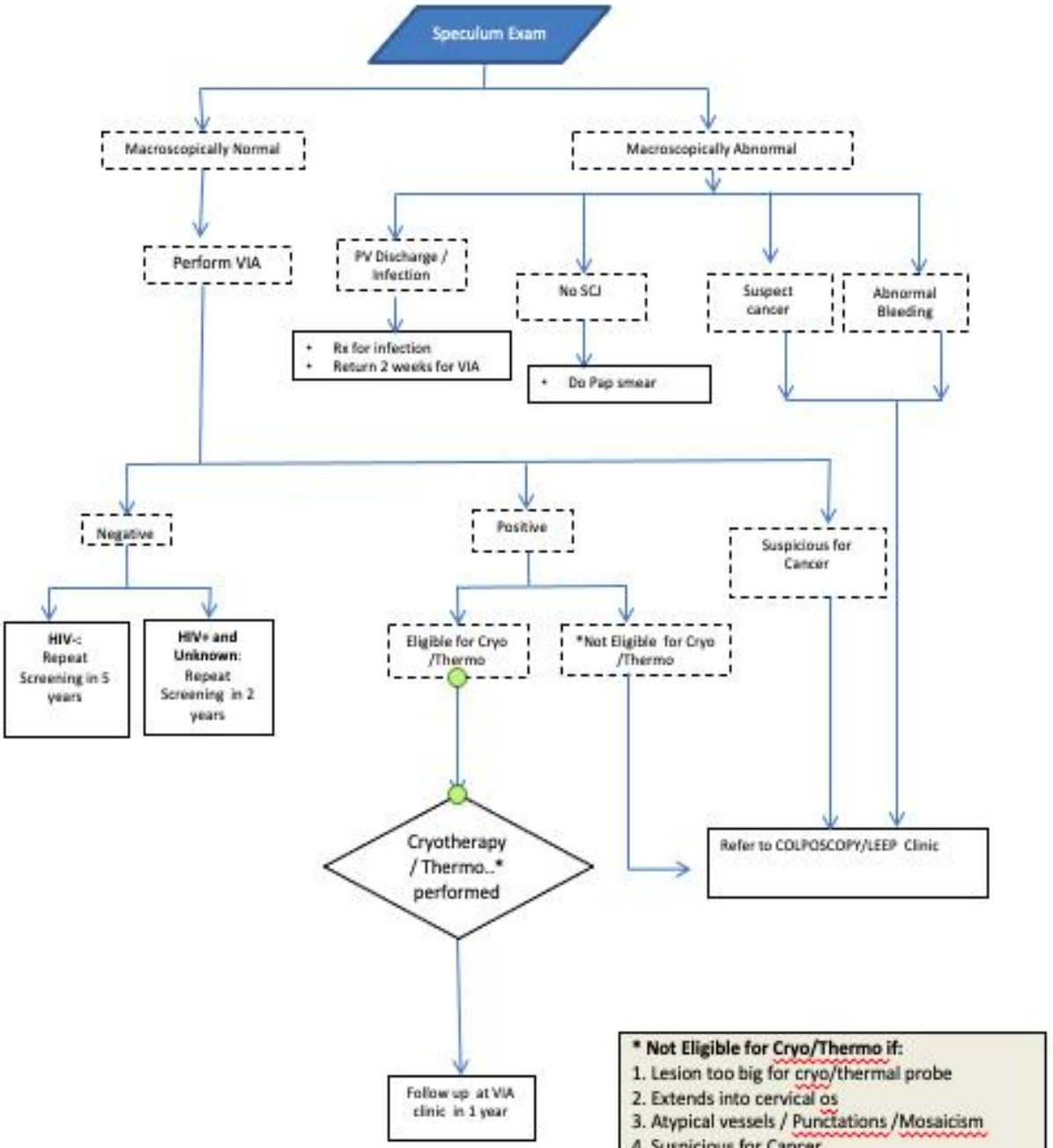
Remember if there is clinical suspicion of cervical cancer,
a definitive diagnosis needs to be made as quickly as possible,
with urgent linkage to cancer treatment as soon as diagnosis is made.

- Refer to current screening and treatment algorithms below for pre-cancer lesion management using the three screening methods.
- Always focus on cervical cancer prevention by becoming familiar with and closely following the algorithm recommendations:

    - Algorithm #1: PAP Smear Results
    - Algorithm #2: VIA Screening
    - Algorithm #3: HPV Screening
    - Algorithm #4: Visual Assessment for Treatment
    - Algorithm #5: Colposcopy/LEEP Visit
    - Algorithm #6: 1 Year after Cryo/Therma or LEEP


ALGORITHM #1
PAP smear results
PAP SMEAR Results
Normal (NILM)
LSIL or ASCUS
Persistent LSIL or ASCUS
ASC-H
HSIL
AGC or AGC-NOS or FN, AIS
AGC/AGUS Abnormal Endometrial Cells OR Normal Endometrial cells in post menopausal women
Cancer SCC or AdenoCA
Repeat Screening 2 HIV+; SHIV- years
Repeat PAP SMEAR after 1 year
Refer for Colposcopy/LEEP Clinic
Refer for URGENT LEEP or Biopsy
Refer Gynae for Endometrial Sampling
PAP SMEAR results after 1 year
Normal (NILM)
LSIL or ASCUS
ASC-H
HSIL
AGC/AGUS/ AIS
Abnormal Endometrial Cells OR Normal Endometrial cells in post menopausal women
Cancer SCC or AdenoCA
Repeat Screening 2 HIV+; SHIV- years
Refer for Colposcopy /LEEP Clinic
Refer for URGENT LEEP or Biopsy
Refer Gynae for Endometrial Sampling

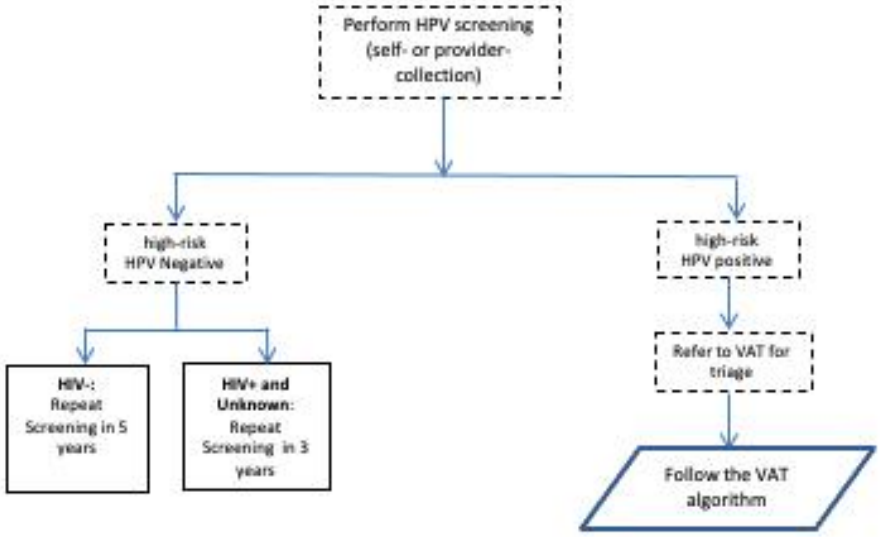
ALGORITHM #2
VIA screening



Consult if unsure at any stage.

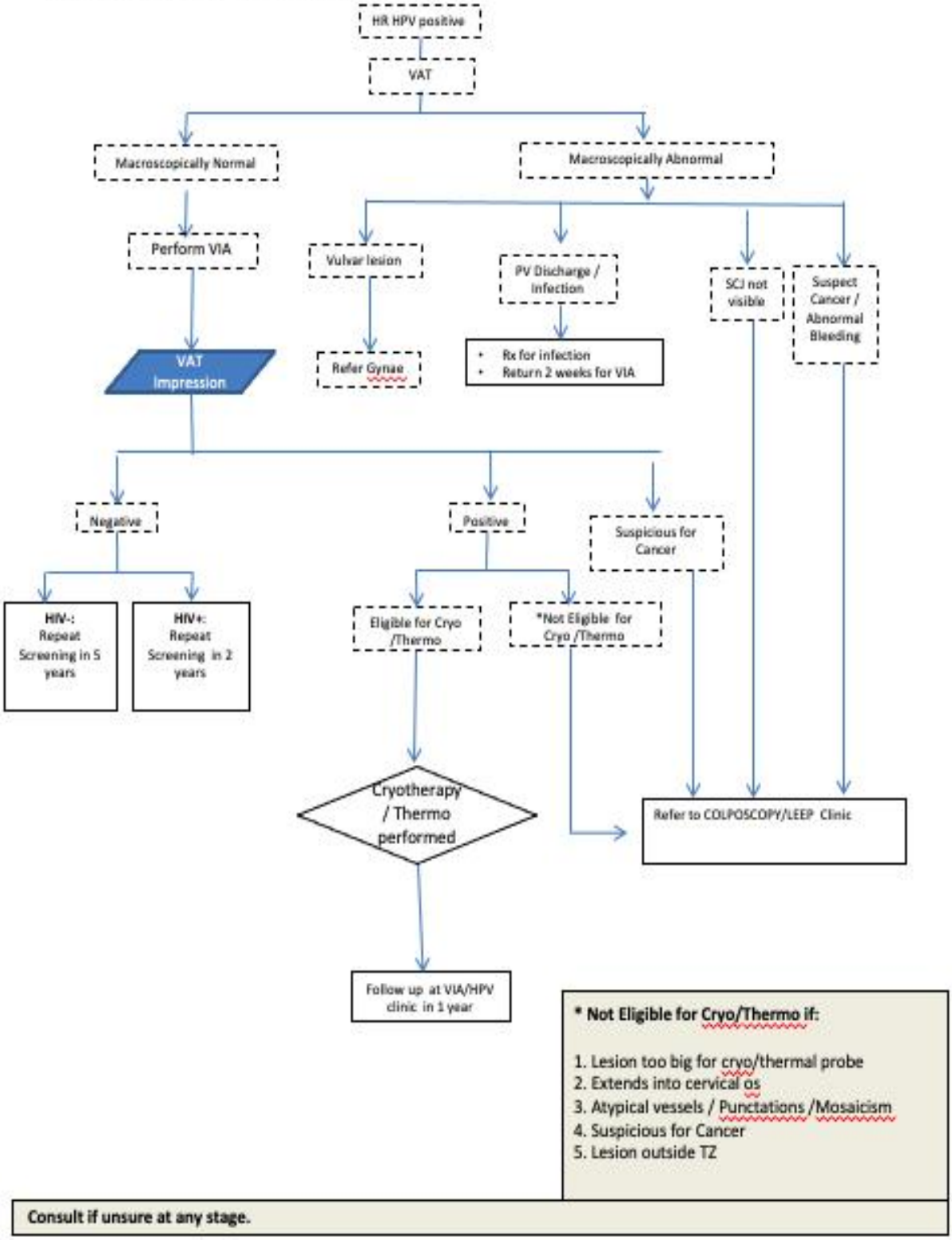
Never turn anyone away. Remember to always examine external genitalia prior to speculum exam. If above screening age do a speculum exam: 1.Lesion suspicious for cancer-refer as above; 2.SCJ fully visualized-perform VIA; SCJ not fully visualized-perform a Pap smear *Repeat thermo ablation as needed to cover the lesion.

ALGORITHM #3
HPV screening

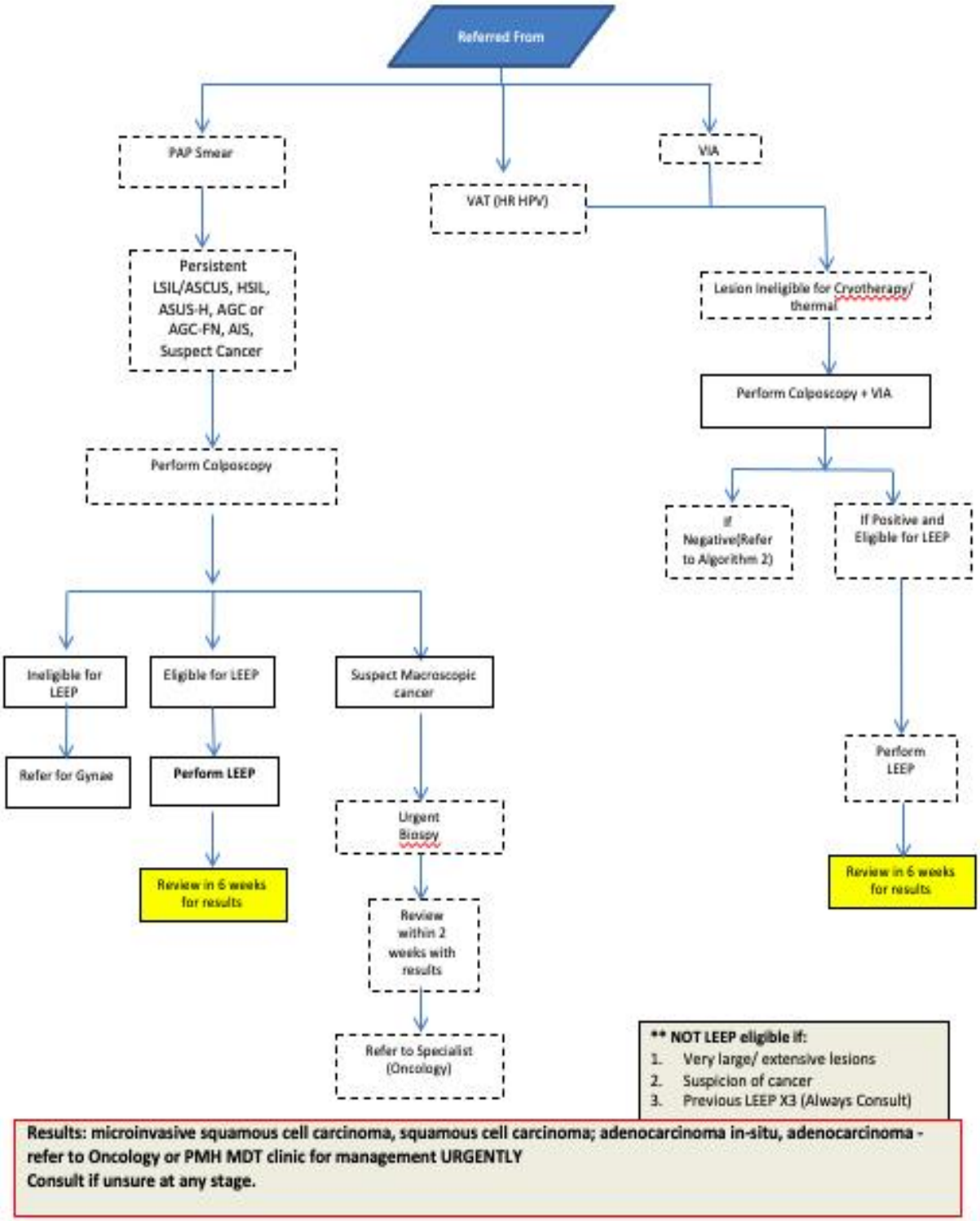


Consult if unsure at any stage.

ALGORITHM #4
Visual assessment for treatment

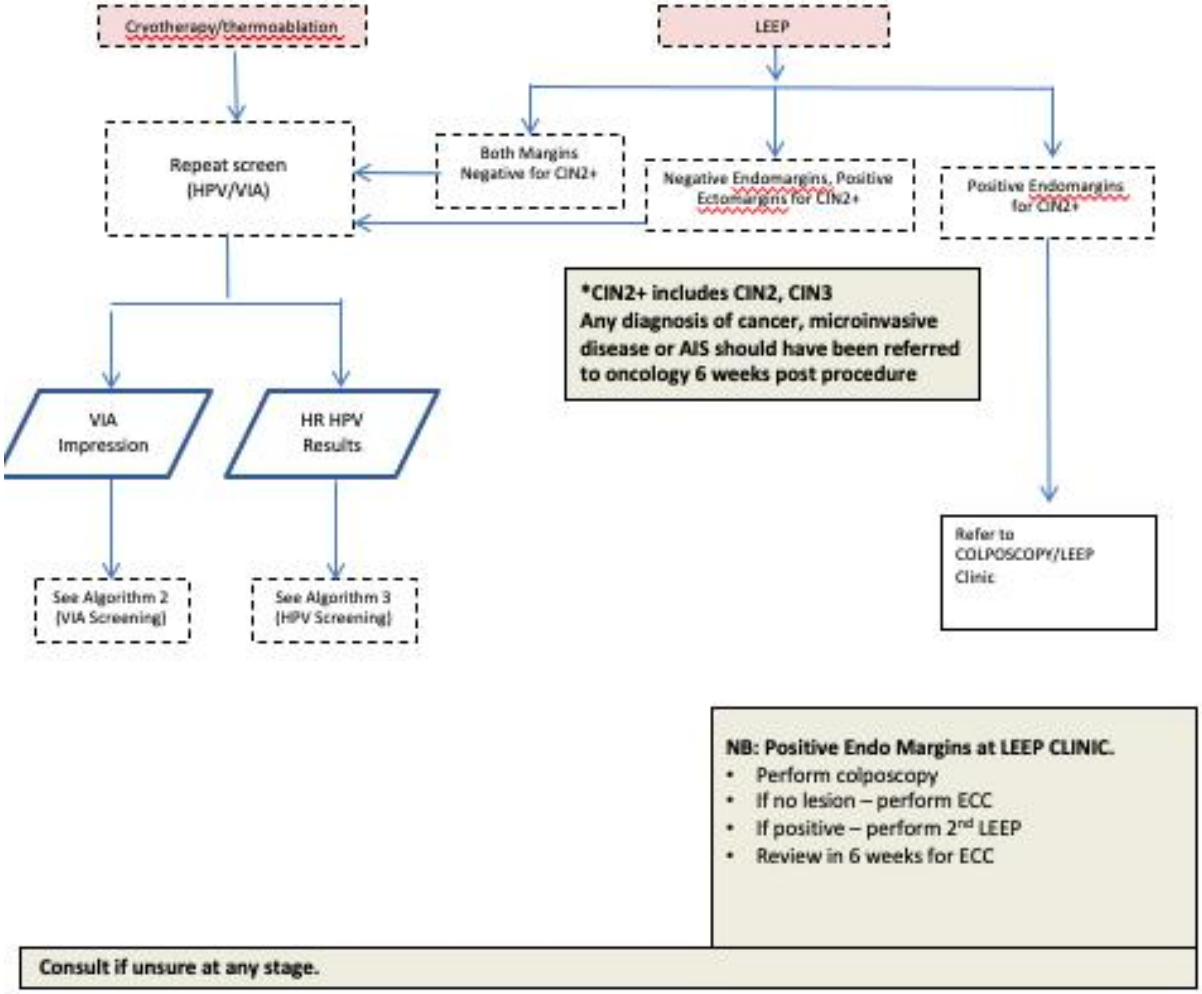


ALGORITHM #5
Colposcopy/LEEP visit



Results: microinvasive squamous cell carcinoma, squamous cell carcinoma; adenocarcinoma in-situ, adenocarcinoma - refer to Oncology or PMH MDT clinic for management URGENTLY
Consult if unsure at any stage.

ALGORITHM #6
1 year after Cryo/thermal or LEEP



ANNEX 1: POST-EXPOSURE PROPHYLAXIS (PEP)

Introduction

PEP is a short course of antiretroviral medicines taken after exposure to HIV to reduce the likelihood of acquiring HIV infection. A person can be accidentally exposed to HIV through healthcare work (occupational exposure) or through such as condom bursts, sexual assault or any unprotected sex.

Initiate PEP within 4 hours of the exposure, and not later than 72 hours.

If started within 72 hours after exposure, PEP can significantly reduce the risk of HIV infection. Adherence to the full course of antiretroviral medication is critical to the effectiveness of the intervention.

Body Fluids and their HIV Infectiousness:

- Body fluids which are infectious for HIV include :
  - Blood, genital and anal secretions, pericardial, pleural, synovial, amniotic, cerebral spinal, ascitic and breast milk
  - Non-infectious fluid 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 and nasal secretions
    However, these fluids may become infectious when contaminated with blood.

Type of Exposure:

- **Percutaneous:** injury causing break in skin and exposure to body fluid, usually via needle (needlestick injury) or scalpel injury.
- **Mucosal:** conjunctival and oral mucous membrane exposure to body fluid.
- Cutaneous: contact of HIV infectious material with a person's skin
- Semen released into vaginal or rectal mucosal as a result of a condom burst.

Exposure Management

- Wash exposed wounds and skin sites with soap and water.
- Flush mucous membranes with water.
- Avoid use of antiseptics, douches, bleach, brushing or flossing (when a condom breaks during oral sex) or other caustic agents, including injection of the exposed site with these agents.

Estimation of the HIV Risk of the Specific Exposure:

- **Needlestick injuries:** The risk of transmission from a needlestick has been estimated at 0.3%, or just about three in a thousand. Transmission rate is greater with a hollow-bore needle, source was person's artery or vein, person's blood or other infectious fluid was visible on the needle, the injury was deep and the patient's viral load was high.
- **Mucous membrane exposure**: Estimated 0.09% risk of HIV transmission. Factors that may affect this risk are the volume of infected fluid, the length of exposure, any exposure management undertaken (e.g., eye washing), and the underlying integrity of the conjunctival or oral mucous membranes (e.g., conjunctivitis, oral ulcers, and obvious breaks in the oral mucosa).
- **Condom Failure/Burst**

It is important to note that the risk of acquiring HIV when condoms burst is not known but assumed to be low. Therefore, every effort should be made to begin PEP as soon as possible and start PrEP if there is more than one episode of condom burst.

- **Cutaneous exposure**: Transmission risk from exposure of HIV-infectious fluid to intact skin is believed to be negligible unless there is underlying dermatitis or significant skin breakage.

Counseling in Cases of a Condom Burst

Individuals who do not know their own or their sexual partner's HIV status are at risk of acquiring HIV when there is condom failure. If a person presents for PEP after a condom failure without knowing the status of their partners and refuse to ask their partners to disclose or test for HIV:

- Administer a rapid HIV test and provide PEP.
- Provide emotional and psychological support and refer for further psychological interventions as needed.

Should couples arrive who do not know their own or their sexual partner's HIV status:

- Administer rapid HIV tests to both.
- If one partner tests positive, refer them for ART initiation.
- Administer PEP to the negative partner(s) and perform follow up HIV testing at the completion of PEP. Be sure to monitor person's outcomes and clearly document their information for tracking purposes.

Individuals who know that their sexual partners are HIV positive but do no their own HIV status must test for HIV with a rapid test. Encourage them to find out the current status of their partner's viral load.

- If their partner's VL is suppressed, there is little chance that a condom failure /exposure will result in HIV infection.
- Once the HIV status of the person is determined and if they are HIV negative, allow them to decide whether or not to take PEP, after counseling on the risk of HIV infection during the "window period."
- If they are found to be HIV positive, refer them for immediate initiation of ART and provide emotional and psychological support, as needed.

Counseling in Cases of Rape or Defilement

Determination of HIV Status of the Exposed Person:

- If the exposed person is already known to be HIV-infected, PEP is not indicated but rather ART. Refer for immediate initiation if needed.
- If the exposed person does not know their HIV status, an HIV self-test or HIV rapid test should be completed, as soon as possible.
- If the exposed person refuses HIV testing, then PEP should not be given.
- If the exposed person tests HIV-positive, then PEP is not indicated but immediate initiation of ART is required.
    - Provide emotional and psychological support and refer for further psychological interventions as needed.

Determination of the HIV Status of the Source Patient:

- If the exposed person is found to be HIV-negative, then the HIV status of the source person must be determined, unless the source person is already known to be HIV-infected.
- If the source person's HIV status is unknown, and if they refuse HIV testing - an HIV Rapid test should be given. The results should not be shared with the source person. If the source person physically hinders or obstructs performance of rapid testing, then it is necessary to initiate PEP for the exposed person.

In spite of all the scenarios described above, remember the ideal time for initiating PEP is within 4 hours and never later than 72 hours!

Decision Whether or not to Initiate PEP:

- Decisions regarding initiation of PEP must be based upon clinical evaluation of each exposure, including the type, the amount of potentially infectious fluid exposed, the potential infectiousness of the fluid, and the HIV status of the source person.

Remember:

- Exposures to fluids not normally infectious for HIV, as listed above, do not always merit PEP, even if the source person is HIV-infected.
- Many mucosal exposures do not merit PEP, especially when the exposure is minimal and the source person is virally suppressed.
- Exposure of intact skin to HIV-infectious fluid does not merit PEP.
- Human bites are not infectious for HIV and do not merit PEP, unless visible blood from the biter was present in the biter's mouth prior to the bite.
- The length of time HIV can survive outside the body is unknown. However, needle stick injuries from devices left in the trash or elsewhere merit PEP.
- An HIV Specialist should be consulted in difficult cases.

In all situations, the decision to initiate PEP must consider the possibility that the source person might be recently infected and is in the "window period". Whenever the practitioner believes there is a reasonable chance that the source patient who tests HIV negative may be in the "window period," PEP should be given.

Initiation of PEP and monitoring

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

PEP must be taken for a full period of 28 days.

The antiretroviral combination recommended for PEP is the same as the first line regimen used for ART. If there is a suspected contra-indication or the infected person is highly treatment experienced, start with the first line regimen and then immediately discuss the case with an HIV specialist.

- For adolescents and adults the recommended PEP regimen is:
  - TAF/FTC/DTG (TAF-ED) *or if not available* TDF/3TC/DTG (TLD)

  If triple therapy is not well tolerated, clinicians may consider dual therapy 3TC/DTG. Discuss such cases with an HIV Specialist, as needed.

- Children who are not eligible to take the above combinations due to weight should start:
  - ABC+3TC+DTG

- Emphasize that the effectiveness of PEP requires completing the full 28 days course.
- Schedule clinical follow-up 2 weeks after PEP initiation to evaluate any side effects and to provide adherence counseling and emotional support.
- Monitor laboratory results of the person on PEP.
- Obtain baseline and follow-up laboratory testing. However, obtaining baseline laboratory tests, must not delay initiation of PEP beyond 4 hours after the incident.
- Pregnancy or breastfeeding is not a contraindication to PEP.
- Counsel the person taking PEP to practice safe sex during the period of PEP and until repeat HIV testing has been completed.
- Educate the person taking PEP about ART side effects. Advise them to return immediately should such side effects appear.
- Consider drug-drug interactions between PEP medications and other medications that the person might be taking, antiepileptics, antacids or other cation containing regimens.

Repeat HIV Testing after PEP:

- The person taking PEP should return for repeat HIV testing at the completion of PEP and at 3 months, after the initial exposure. If 4th generation HIV test kits are available HIV testing can take place as soon as 2 weeks after exposure.
- For women who chose to cease breastfeeding while on PEP: Confirm negative status at the completion of PEP to allow resumption of breastfeeding. If 4th generation HIV testing kits are available HIV testing can take place within 2 weeks.

All of the above steps must be carefully documented in the manual and electronic medical records of the person taking PEP.

PEP and Other Indicated Care for Victims of Sexual Violence:

Victims of rape, sodomy, and defilement—including infants and children—who present for care within 72 hours of the incident should be offered PEP. *(see Section 1.2.5)*

- Even if the perpetrator tests HIV-negative, the result must be interpreted with caution, as it is possible that the perpetrator is in the "window period."
- The practitioner must not wait for a police report before initiating PEP and is not bound by any police report in determining the need for PEP
- It is essential that police understand that PEP must be started immediately for victims of sexual violence; therefore, victims of sexual violence must first be brought to the hospital or clinic for PEP evaluation before a detailed police interrogation is initiated.
- 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 sexual abuse to the police once PEP has been initiated.
- Victims of sexual violence, especially children, require special medical and psychosocial care. Although appropriate referrals for this care may be necessary, the treating clinician must also provide such care, and not merely delegate it. Moreover, this care should be given regardless of whether or not the victim receives PEP, as follows:
  - Empiric treatment for other STIs which may have been transmitted during the sexual abuse should be administered.
  - Offer women of sexual reproductive age, emergency contraception in the forms of "morning after pill" to prevent pregnancy.
  - If genital/rectal trauma has occurred, promptly refer the patient for appropriate surgical, urological, or gynecological care, as indicated.
  - Obtain baseline, 4 weeks and 3 months HIV rapid tests, and if positive, initiate appropriate support and referrals.

- Depression, shame, guilt, and suicide have followed rape or other forms of sexual abuse, so ongoing psycho-social interventions and counseling are required, including referral for evaluation.
- Since the psychological trauma of rape may not be evident at the initial visit, such interventions must be ongoing at follow-up visits, and should always be conducted within a safe, supportive, and confidential environment.

ANNEX 2: TESTING ALGORITHM FOR CONFIRMATORY HIV TESTING USING DETERMINE & UNIGOLD TESTING KITS

Table 1: Testing Algorithm for Confirmatory HIV Testing using Determine & Unigold Testing Kits

HIV Testing Algorithm ≥18 months of age
Perform testing with the first rapid HIV test (T1 -Determine) for HIV screening ↓
If T1 (Determine) is negative, the client is diagnosed as HIV negative, Recommend annual HIV testing and refer the client to the appropriate HIV prevention services. *(see section XXX for HIV combination prevention services)*
↓ If T1 is positive, repeat with a second rapid HIV test (T2-Unigold)
If T2 (Unigold) is positive, repeat with a third rapid HIV test (T3) ↓
If T1, T2 are all positive The client is diagnosed as HIV positive and immediately refer and track the client to an ART initiation site.
If T1 (Determine) is Positive but T2 (Unigold) is Negative ↓ Repeat both T1 (Determine) & T2 (Unigold)
If the tests remain discordant **Report both of these results as inconclusive** Send for PCR immediately and ask the patient to Return in 7 days for the result.
Notify the National Reference Lab (BHHRL-Gaborone: 3902671 FT: 2441917) & The National HIV Testing Programme (3632313)
NOTE: The implementation of 4th Generation HIV Testing will begin in 2023 and these algorithms will be revised.

ANNEX 3: HIV SPECIALIST DIRECTORY

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ANNEX 4: KEY POINTS FOR COMMON METHODS OF CONTRACEPTION IN BOTSWANA

Contraceptive options for PLWH: Women living with HIV can use all currently available contraceptive methods so there are many options that providers can help patients to choose from, each with advantages and disadvantages. A woman's reproductive health needs are dynamic and change throughout her life course, and so individuals should be supported to make an informed choice about the contraceptive method that would work best for them at that time and supported to switch methods if needed.

Always advise all women that as well as the contraceptive method they choose, the additional use of a male or female condom will protect against the risk of HIV infection/transmission and STIs.

Key points for common methods of contraception in Botswana, including HIV considerations:

Copper Intrauterine Device (Cu IUD, 'loop')

- **Mechanism of action:** It inhibits fertilization through effect of copper on sperm and ovum.
- **Length of contraception**: 10-12 years (or 5 years, depending on type)
- **Effectiveness:** >99% effective
- **Advantages:** Highly effective, long acting, reversible method of contraception (LARC); non-hormonal, non-user-dependent, can also be used as emergency contraception
- **Disadvantages:**
    - Requires procedure for insertion with associated small risk of uterine perforation or infection (PID);
    - Requires trained provider for insertion so it may not be available to initiate same day.
    - Periods may be heavier or more painful for first few months;
    - Risk of ectopic pregnancy if pregnancy with Cu IUD in situ (but overall, significantly lower risk of ectopic pregnancy compared to a woman not using contraception)
- **HIV considerations:** generally safe, delay insertion if current PID/STI, avoid if pelvic TB and some malignancies are present.

Levonorgestrel intrauterine system (LNG-IUD)*

- **Mechanism of action:** Thickens cervical mucus, thins the endometrium.
- **Length of contraception:** 5 years (Mirena®) or 3 years (Jaydess®)
- **Effectiveness:** >99% effective
- **Advantages:** Highly effective, long-acting, reversible method of contraception (LARC), non-user dependent; few clinic visits required. May improve dysmenorrhea and menorrhagia symptoms, including in patients with endometriosis.
- **Disadvantages:** Requires procedure for insertion with associated small risk of uterine perforation or infection (PID); requires trained provider for insertion so it may not be available to initiate on the same day. Changes to bleeding pattern (amenorrhea/spotting/prolonged periods) most common side effect.
- **HIV considerations:** generally safe, delay insertion if current PID/STI, avoid if pelvic TB and some malignancies present. Potential for drug interactions with some ART/TB medications

**Currently only available in the private sector in Botswana*

Implant

- **Mechanism of action:** Suppresses ovulation & thickens cervical mucus.
- **Length of contraception:** 5 Years (Jadelle®) or 3 years (Implanon NXT®)
- **Effectiveness:** >99.9% effective
- **Advantages:** Highly effective, long acting, reversible method of contraception (LARC); non-user-dependent, few clinic visits required.

- **Disadvantages:** Requires procedure for insertion by trained provider with associated small risks of pain/bleeding/infection; changes to bleeding pattern (spotting/irregular periods/amenorrhea/prolonged bleeding) most common side effect – good counselling required on how to manage this.
- **HIV considerations:** Safe and effective; potential for drug-drug interactions with some ART and TB medications

DMPA 3-Monthly Injectable

- **Mechanism of action:** Suppresses ovulation, thickens cervical mucus.
- Length of contraception: repeat injection required every 13 weeks for ongoing contraception cover.
- **Effectiveness:** >99% Effective with perfect use; ~94% effective with typical use.
- **Advantages:** Effective, not visible (private), few drug-drug interactions.
- **Disadvantages:** More user-dependent, changes to bleeding pattern (amenorrhea, spotting/irregular periods/prolonged bleeding), weight gain, reversible reduction in bone mineral density; return to fertility may be delayed (up to 12 months after discontinuation).
- **HIV considerations:** Safe and effective, no increased risk of HIV acquisition. Avoids drug-drug interactions with certain ART and TB medications.
- A large randomized clinical trial (the Evidence for Contraceptive Options and HIV outcomes (ECHO) study, published in 2019), showed that no method of contraception substantially increased the risk of HIV acquisition. Therefore, there is no evidence that DMPA injection increases the risk of an HIV-uninfected woman acquiring HIV. Therefore, there should be no restrictions on the use of DMPA for women living with HIV or women at high risk of HIV.

Combined Oral Contraceptive pill (COCP)

- **Mechanism of action:** Suppresses ovulation, thickens cervical mucus.
- **Length of contraception**: 21-day cycle with 7-day pill-free (or placebo pill) break. Short-acting method – pill must be taken every day at the same time (within 12 hours).
- **Effectiveness:** >99% Effective with perfect use; ~91% effective with typical use.
- **Advantages:** Easy to start and stop, regulates periods and may improve symptoms of dysmenorrhea or menorrhagia; may help with symptoms of polycystic ovarian syndrome or endometriosis.
- **Disadvantages:** User-dependent, reliant on near-perfect adherence to provide good contraceptive cover, contraindicated in greater number of medical conditions, small but significant risk of severe side effects including venous (deep vein thrombosis, pulmonary embolus) and arterial (stroke, myocardial infarction) thrombosis.
- **HIV considerations:** Safe and effective, potential for drug-drug interactions with some ART and TB medications.

Progestin-Only Pill (POP)

- **Mechanism of action:** Suppresses ovulation, thickens cervical mucus.
- **Length of contraception:** 28-Day cycle, no pill-free break. Short-acting method – pill must be taken every day at the same time (within 2 hours).
- **Effectiveness:** >99% Effective with perfect use; ~91% effective with typical use.
- **Advantages:** Easy to start and stop, safe to use in wider range of medical conditions than COCP
- **Disadvantages:** User-dependent, reliant on near-perfect adherence to provide good contraceptive cover, changes to bleeding pattern (spotting/amenorrhea/irregular periods/ prolonged bleeding) common.
- **HIV considerations:** Safe and effective, potential for drug-drug interactions with some ART and TB medications.

Condoms (male and female)

- **Mechanism of action:** Mechanical barrier to prevent exchange of fluid and semen.
- **Length of contraception**: Single use with each episode of sexual intercourse
- **Effectiveness:** 98% effective with perfect use; ~82% effective with typical use.

- **Advantages:** The only contraceptive method that reduces STI and HIV acquisition, non-hormonal
- **Disadvantages:** User-dependent, reliant on perfect adherence to provide good contraceptive cover, risk of breakage/user error
- **HIV considerations:** The only contraceptive method that prevents HIV/STI acquisition.

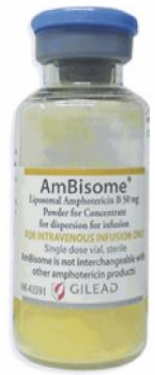
Male and Female Sterilization

- **Mechanism of action:** Cutting and/or sealing of the vas deferens to prevent passage of sperm to the urethra (male sterilization); or cutting and/or sealing of the fallopian tubes to prevent passage of an egg from the ovaries (female sterilization), thereby preventing fertilization.
- **Length of contraception:** Permanent, should be considered irreversible (reversal procedures are available but are not always effective).
- **Effectiveness:** >99% effective
- **Advantages:** Permanent, for couples who have completed their families; non-hormonal
- **Disadvantages:** Requires surgical procedure with associated risks, risk of one or both partners changing their mind and wanting other children in future.
- **HIV considerations:** Safe and effective, avoids drug-drug interactions.

ANNEX 5: LIPOSOMAL AMPHOTERICIN & FLUCYTOSINE DOSING AND OTHER INFORMATION FOR TREATMENT

Table 1: Liposomal Amphotericin Reconstitution Dosing

Ambisome
10 mg/kg D1



Patient's weight	Number of vials	Total dose of AmBisome	Volume of reconstituted AmBisome (ml) at 4mg/ml	Additional dextrose (ml) to create a 1litre total infusion
40 kg	8	400 mg	100 ml	900 ml
41-45 kg	9	450 mg	112.5 ml	887.5 ml
46-50 kg	10	500 mg	125 ml	875 ml
51-55 kg	11	550 mg	137.5 ml	862.5 ml
56-60 kg	12	600 mg	150 ml	850 ml
61-65 kg	13	650 mg	162.5 ml	837.5 ml
66-70 kg	14	700 mg	175 ml	825 ml
71-75 kg	15	750 mg	187.5 ml	812.5 ml
76-80 kg	16	800 mg	200 ml	800 ml
81-85 kg	17	850 mg	212.5 ml	787.5 ml
86-90 kg	18	900 mg	225 ml	775 ml

Ambisome should NEVER be mixed with Normal Saline or Half Normal Saline as it will precipitate. The line that is used for Ambisome should not be used for administering any other drugs.

Ambisome comes in a 50 mg vial. Reconstitute by adding 12 ml sterile water to each vial and immediately shake vigorously for 30 seconds until all particulate matter has dissolved (becomes translucent and yellow).

Remove an equal volume of reconstituted Ambisome from the 1L of 5% Dextrose (e.g., if the patient is receiving 500mg of Ambisome, the reconstituted volume of Ambisome will be 125ml, therefore remove 125ml from a litre of dextrose, which shall be replaced by the Ambisome).

Always use the provided filter in the packaging to transfer the Ambisome into the bag of dextrose, to avoid any particulate matter getting through to the patient. Once the Ambisome is instilled into the bag of dextrose, gently shake and mix well.

The infusion must be given **over 2 hours and not faster** otherwise it can cause cardiac problems. It is not required to cover the bag or the giving set as the drug will not be degraded by sunlight in the period that it is infused.

Table 2: Guidance on Flucytosine Dosing

Weight (kg)	Daily dose (mg) 100mg/kg	Number of tablets per day	Suggested schedule of dosing*			
35-39	3500	7	2	2	2	1
40-44	4000	8	2	2	2	2
45-49	4500	9	3	2	2	2
50-54	5000	10	3	2	3	2
55-59	5500	11	3	3	3	2
60-64	6000	12	3	3	3	3
65-69	6500	13	4	3	3	3
70-74	7000	14	4	3	4	3
75-79	7500	15	4	4	4	3
80-84	8000	16	4	4	4	4

*Flucytosine tablet dose - 500mg

Table 3: Flucytosine Dosing for Renal Toxicity

Creatinine clearance ml/min	Individual dose mg/kg	Dose interval hour
>40	**25**	**6**
40-20	**25**	**12**
20-10	**25**	**24**
<10	**25**	**>24**

Table 4: Flucytosine Dosing for Bone Marrow Toxicity

Neutrophils	$0.4x\ 10^9$ to $0.59\ x\ 10^9$	Monitor FBC daily. If in this range, confirm neutrophil count the next day, if remains in this range halve dose of flucytosine (50%)
	$< 0.4x\ 10^9$	Stop flucytosine, until neutrophils are above 0.4 at which point resume at 50% dose
Platelets	$25\ x\ 10^9$ to $< 50\ x\ 10^9$	Monitor FBC daily. If in this range, confirm platelets count the next day, if remains in this range halve dose of flucytosine (50%)
	$< 25\ x\ 10^9$	Stop flucytosine, until platelets are above 25 at which point resume at 50% dose

Table 5: Recommended Lab Monitoring Schedule for Single, High-Dose LA Regimen

INVESTIGATION	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14
Diagnostic LP	X													
FBC	X						X							
Renal Function	X			X										
ALT	X						X							

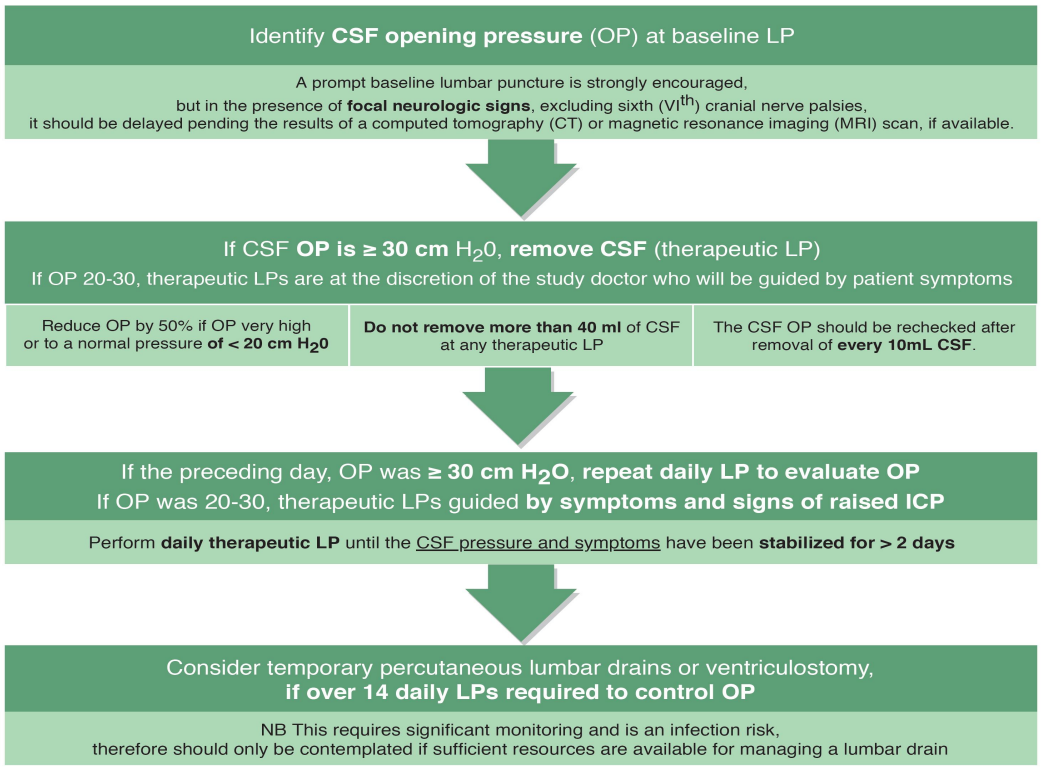
If abnormal/borderline baseline bloods repeat sooner

Table 6: Recommended Lab Monitoring Schedule for 1 Week Amphotericin B Regimen

INVESTIGATION	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14
Diagnostic LP	X													
FBC	X						X							
Renal Function	X		X		X		X			(X)*		(X)*		
ALT	X						X							

*Perform if patient is still an inpatient.
If day 7 FBC shows anemia repeat Hb during second week of treatment.

Figure 1: Raised ICP Management



ANNEX 6: DIFFERENCES BETWEEN LATENT & ACTIVE TB

Table 1: Difference between Latent TB infection & Active TB Disease

Latent TB infection	Active TB disease
No symptoms suggestive of TB disease	One or more of the following symptoms: fever, cough, weight loss, night sweats, VL ›200 copies/µL, often CD4 ‹200 cells/µL.
TB blood test or TST result usually positive.	TB blood test or TST result may be positive or negative.
Chest radiograph is typically normal.	Chest radiograph is usually abnormal but may be normal in people with advanced HIV (i.e., CD4 ‹200 cells/ µL).
GeneXpert and culture negative	Usually GeneXpert and/or are culture positive, but may also be negative, particularly in HIV positive patients.
Cannot spread TB bacteria to others.	Can spread TB bacteria to others and require ATT.
Should be given TPT if eligible.	Should be given treatment for active TB disease according to TB treatment guidelines

Patients eligible for TPT will be identified through intensified case finding at IDCC and active case finding through contact investigation.

Table 2: Interpretation of Xpert MTB/Rif Results

Interpretation of Xpert MTB/Rif Results

	Xpert MTB/Rif Results	Interpretation
Positive for TB	• MTB detected, • No RIF resistance detected	• Sensitive to rifampicin
	• MTB detected, • RIF resistance detected	• Resistant to rifampicin, Probable MDR-TB
	• MTB detected, • RIF resistance indeterminate	• No results available for rifampicin resistance
Negative for TB	• MTB not detected	• Can't not rule out EPTB
Invalid/Error		• No Xpert results reported

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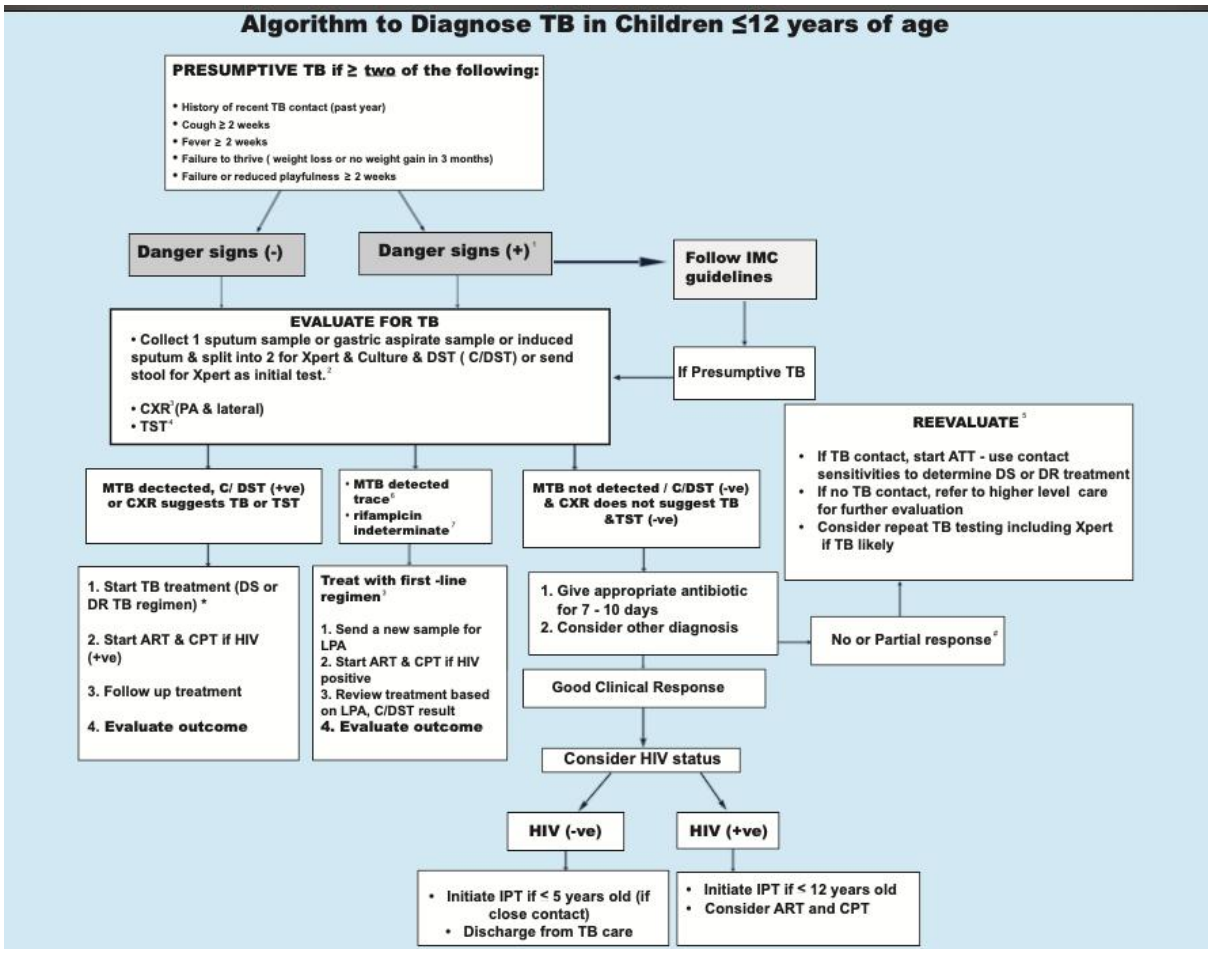
ANNEX 7: ALGORITHM TO DIAGNOSE TB IN CHILDREN < 12 YEARS



NOTES

1. IMCI Danger signs: lethargy, unconscious, inability to feed or breastfeed, vomiting everything

2. If child cannot produce sputum, collect 1 gastric aspirate or 1 induced sputum sample and split for genexpert and culture(2 ml each) or send stool for Xpert. If high suspicion for resistance send aspirate or sputim for culture in addition to stool testing Bacterial confirmation should always be saught but is not essential before starting ATT. Refer TB manual for details on gastric aspirates and sputum induction

3.CXR findings suggestive of TB include any one of the following: hilar adenopathy, infiltrates, airway compression, pericardial effusion, pleural effusion

4.TST –refer to TB manual for details of performing TST

5. Remember that infants are at extremely high risk for TB, following documented exposure and symptomatic children under 5 years old should preferably be assessed by a doctor

6. MTB detected trace results do not provide any information regarding rifampicin susceptibility or resistance.

7. Patients should be initiated on a first-line regimen according to national guidelines unless the patient is at very high risk of having MDR-TB or if a second Ultra assay indicates rifampicin resistance. Such patients should be initiated on an DR-TB regimen.

Genexpert Results

MTB detected/No rifampicin resistance
• Start DS TB regimen if no TB treatment history
• Follow up culture results
MTB detected or trace/Rif resistance indeterminate or unknown
• Send another sample for repeat Xpert
• *While waiting start DS 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.

+ MDR Contact or Culture with Resistance

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

ANNEX 8: PHARMACOVIGILANCE

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. The aims of PV are to enhance patient care and patient safety in relation to the use of medicines and to support public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines.

Benefits of Pharmacovigilance

A robust PV program on the use of antiretroviral medications will:

- Encourage the prudent, rational, and effective use of ARV medications and to strengthen patient care, safety and public health.
- Promote understanding, education, and clinical training in PV as well as effective communication of medicine safety to PLHIV and the community at large to build public trust.
- Monitor and assess the risk-benefit balance of the medicines used in the program to further inform treatment and case management decisions.
- Detect rare and unexpected adverse reactions that may not have been identified during clinical trials as well as to detect any new potential signals.
- Generate information on the incidence, severity, and nature of adverse events from HIV medications.

Any ADR a patient experiences while on ARV therapy should be reported, this includes:

- All known or unknown, serious, or unserious, mild to severe adverse event or any discomfort that a patient reports.
- All ADRs associated with drug-drug, drug-food or drug-supplements (including herbal or complementary) interactions.
- ADRs occurring from an overdose or medication error.
- Off-label use of drugs.
- Abnormal changes in laboratory tests suspected to be caused by an ADR.

Monitoring of Adverse Drug Reactions (ADRs) should be integrated as standard of care to accompany the routine practice of monitoring treatment outcomes. At every encounter between a healthcare professional (HCP) and a patient, the HCP should screen for any ADRs, manage and report to Botswana Medicines Regulatory Authority (BoMRA) and appropriate clinical supervisors.

Reporting Adverse Drug Reactions

HCPs are expected to report both non-serious and serious ADRs to BoMRA.

- **All non-serious ADRs** must be reported within 15 calendar days of discovery.
- **All** serious ADRs must be reported within 72 hours, so that causality assessment are carried out and appropriate regulatory measures taken.
    - **A serious ADR is defined as:** Any event that is: fatal, life-threatening, permanently/significantly disabling, requires or prolongs hospitalization, causes a congenital anomaly, or requires intervention to prevent permanent impairment or damage.

ADR Reporting Platforms

Report all suspected ADR that may be due to any medication to BoMRA using any of the following BoMRA platforms:

1. **ADR reporting forms (see page 113 below).**

- You may download the forms from the BoMRA website www.bomra.co.bw and email the completed for to reportadr@bomra.co.bw

2. **E-reporting.**

- Follow the Primary eReporting (who-umc.org) link available on BoMRA website and complete the form online.
- BoMRA Regulatory Information Management System (BRIMS) Portal (bomra.co.bw) https://brims.bomra.co.bw/#/public/app-home

3. **MedSafety App**

- Use the ADRs reporting App, available on apple store or google store for smart phones

4. **Call BoMRA at 373 1727/ 20**

5. **For more information about any medicine/vaccine safety contact, BoMRA National Medicines Information Centre at 373 1788/71 or email nmic@bomra.co.bw**

ADR Reporting Form

Botswana Medicines Regulatory Authority

BOMRA/PCT/PV/P01/F01 **Suspected Adverse Drug Reactions Reporting Form** Issue No.1

SUSPECTED ADVERSE DRUG REACTIONS REPORTING FORM

I. Patient Information:

Patient initials: Reference No:	Sex: M ☐ F ☐	Date of Birth or Age (yrs) (dd/mm/yyyy)
Date of last menstruation:(dd/mm/yyyy)	Weight (kgs):	

II. Suspected Medication(S)/Vaccine/Herbal:

Medicine/Vaccine (please use **Brand** Names and batch number if known)	Route	Dose	Frequency	Date Drug		Reasons for Use
				Started	Stopped	

III. Other Medicine(S)/Vaccine(s) taken at time of reaction

Medicine/Vaccine (please use **Brand** Names and batch number if known)	Route	Dose	Frequency	Date Drug		Reasons for Use
				Started	Stopped	

IV. Adverse Reaction Experienced/Observed:

Date of onset of Reaction: (dd/mm/yyyy)	Reaction Subsided after Suspect Drug discontinuation: Yes ☐ No ☐	Rechallenge Yes ☐ No ☐
		Outcome:

Description of Adverse Drug Reaction:
(including laboratory test results)

Seriousness: Life threatening ☐ Hospitalized ☐ Congenital anomaly/birth defect ☐

Disabling/incapacitating ☐ Death ☐ Others ☐

Treatment for Reaction:

Outcome: Recovered ☐ Recovering ☐ Not Recovered ☐ Fatal ☐ Recovered with sequelae ☐ Unknown ☐

Date: (dd/mm/yyyy)

Other Pre- existing medical conditions: (E.g. Allergies, Pregnancy, Smoking, Alcohol, Hepatic/Renal Dysfunction, others) -

Additional Information: (if any) -

V. REPORTER:

Name: _____.

Occupation & Specialty._____ Telephone: _____ Health Facility:_____.

Signature: _____ Email address:_____ Address:_____ .

Date: _____.

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Confidentiality: **The patient confidentiality is fully held in strict confidence and protected. Submission of the report does not constitute an admission that the medical personnel, manufacturer, or the product caused or contributed to the reaction. Submission of the ADR report does not have any legal implication on the reporter.**

ADR Reporting Guide

How to complete this form:

ALL FIELDS MUST BE COMPLETED

I. **Patient Details** – Reference number (Case No./Patient No/File No. for your facility DO NOT USE NATIONAL ID NO.)
II. Suspected medicines/Vaccines/Herbal -See an example below
III. Other Medicine(S) Vaccine(s) taken at time of reaction – See an example below

ANNEX 9: The 2022-2025 HIV CLINICAL CARE GUIDELINES COMMITTEE

The following individuals generously contributed to the development of these Guidelines.

2022-2025 HIV CLINICAL CARE GUIDLIINES COMMITTEE MEMBERS *(in Alphabetical Order)*				
	FIRST NAME	SURNAME	SPECIALITY	ORGANISATION
1	Motswedi	Anderson	Hepatitis	BHP
2	Ava	Avalos	HIV, HIV-DR	Careena Centre for Health
3	Jerry	Bolebantswe	ART Programme	MoH: ARV Programme
4	John	Chambo	DHMT	Scottish Livingston Hospital
5	Diana	Dickinson	Peds, HIV, HIV-DR	Independence Surgery
6	Eldah	Dintwa	Prevention, PMTCT	MoH: PMTCT
7	John	Fararai	Pediatrics	Baylor Pediatric Center of Excellence
8	Tendani	Gaolatlhe	HIV, HIV-DR, COVID, Medicine	BHP & UB
9	Joe	Jarvis	Cryptococcus	BHP & UB
10	Max	Kapanda	HIV, Aging	MoHL ARV Programme
11	Joyce	Kgathwane	Pharmacy	UB
12	Botshelo	Kgwaadira	TB/HIV, MDR-TB	BUMMHI
13	Peter	Kuylsteke	Cancer/HIV	UB & Princess Marina Hospital
14	Mpho	Letebele	HIV	CDC/PEPFAR
15	Tebogo	Madidimala	HIV	WHO
16	Jessica	Mafa- Setswalo	PMTCT	MoH: PMTCT
17	Queen	Nthusang	PMTCT	MoH: PMTCT
18	Mogomotsi	Matshaba	Pediatrics	Botswana- Baylor COE
19	Mpho	Mmelesi	Strategic Information	UNAIDS
20	Chawangwa	Modongo	TB, MDR-TB	Global
21	Tuduetso	Molefi	TB	MoH: BNTP
22	Stanley	Monageng	Community	Citizen Activist
23	Milton	Montebatsi	Programmatic	BUMMHI
24	Mosepele	Mosepele	Infectious Disease	BHP & UB
25	Chelsea	Morroni	SRH	BHP & BSRHI
26	Julius	Mwita	Cardiology	UB & Princess Marina Hospital
27	Bornapate	Nkomo	Public Health	MoH: Public Health Specialist
28	Julia	Ngidi	Laboratory	National Laboratory
29	Dinah	Ramaabya	ART Programme	MoH: HIV
30	Vivian	Sebako	Pharmacy	CMS
31	Malema	Sefalani	SRH	MoH-BNTP
32	Partha	Gurumurthy	Pharmacovigilance	BoMRA
33	Lynn	Tjirare	ART Programme	MoH: HIV

Additional Thanks to following individuals: Dr. Tshepo Leeme (BHP), Dr. Samba Nyirendra (Sarai Holistic Care), Dr. Mpelo Mokgwathi, Vasilisa Tabak & Mia Lebanna (Careena), Mr Pono Pono (BoMRA) Dr. Billy Tsima (UB), Kusi Kemmonnye (STI – MoH), Pontsho Pono (ARV Programme MoH), Goabaone Panky Mogomotsi (HTS – MoH), Dr. Leyla Baghirova, & Koorileng Kesalopa & Boineelo Mfundisi (National Laboratory).