



Republic of Zambia
Ministry of Health

DOXY-PEP IMPLEMENTATION GUIDE

Directorate of Infectious Diseases

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DOXY-PEP IMPLEMENTATION GUIDE

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Acronyms

ALT	Alanine aminotransferase
AST	Aspartate Amino Transferase
ART	Antiretroviral Therapy
CAB	Cabotegravir
CAB-LA	Long-acting injectable Cabotegravir
CBP	Community-Based Provider
FSW	Female Sex Worker
HIV	Human Immunodeficiency Virus
HBV	Hepatitis B virus
HBsAg	Hepatitis B surface antigen
HCV	Hepatitis C Virus
HCW	Health Care Worker
PK	Pharmacokinetics
PrEP	Pre-Exposure Prophylaxis
RPR	Rapid Plasma Reagin
STI	Sexually Transmitted Infection
TPHA	Treponema Pallidum Hemagglutination Assay
TWG	Technical Working Group
VMMC	Voluntary Medical Male Circumcision
WHO	World Health Organization
ZAMMSA	Zambia Medicines and Medical Supplies Agency

Foreword



Sexually Transmitted Infections (STIs) remain a significant public health challenge, with rising incidence rates globally and nationally. Innovative, evidence-based strategies are essential to reduce transmission, prevent complications, and support sexual health across diverse communities.

In recent years, the use of Doxycycline as a Post-Exposure Prophylaxis (PEP) strategy has emerged as a promising tool in STI prevention, particularly among populations at higher risk of bacterial STIs such as *Chlamydia trachomatis*, *Neisseria gonorrhoea*, and *Treponema pallidum*. Clinical trials have demonstrated its potential to reduce the burden of these infections when used appropriately and supported by comprehensive sexual health services.

This implementation plan outlines the rationale, operational approach, and key considerations for integrating Doxycycline-PEP (Doxy-PEP) into existing sexual health frameworks. It is informed by current scientific evidence, expert consensus, and a commitment to equity, safety, and person-centered care. Our goal is to ensure that this intervention is delivered effectively, ethically, and sustainably – enhancing STI prevention efforts and supporting the overall well-being of individuals and communities.

We acknowledge that successful implementation depends on the collaboration of healthcare providers, public health professionals, community organizations, and the people we serve. As such, this document is both a guide and a call to action: to innovate responsibly, respond to emerging data, and prioritize the health and dignity of all.

A blue ink signature of Hon. Dr. Elijah J. Muchima, MP.

Hon. Dr. Elijah J. Muchima, MP
Minister of Health

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1.0 Background

1.1 Global Epidemiology of STIs

Globally, there has been an increase in the incidence of various Sexually Transmitted Infections (STIs). According to the World Health Organization (WHO), globally, an estimated 1 million STIs are acquired every day. These infections occurred in individuals aged 15 to 49 years (WHO, 2022). In 2020, there were an estimated 374 million new cases of curable STIs (chlamydia, syphilis, gonorrhoea, and *Trichomonas vaginalis*) in individuals aged 15-49 years, of which 8 million were new syphilis infections among the same age group in 2022 (WHO, 2022). The age standardized incident rate of syphilis increased from 160.03/100,000 in 1990 to 178.48/100,000 in 2019 (Tao *et al.*, 2023). The global burden of STIs tends to be highest in sub-Saharan Africa and Latin America.

High risk and priority populations have been disproportionately affected by STI's. Factors contributing to this include lack of fear of HIV due to frequent use of Pre-Exposure Prophylaxis (PrEP), inconsistent condom use, having multiple concurrent sexual partners, alcohol and substance abuse, use of sexual stimulants and mental health issues.

1.2 Epidemiology of STIs in Zambia

Zambia is one of the countries in Sub-Saharan Africa with a high burden of STIs. In 2023, the number of new cases of syphilis increased to 91,078 from the 63,106 cases of syphilis that were reported in 2022. Among pregnant women attending ANC, 3.6% tested positive for syphilis in 2022. This increased to 5.1% in 2023. According to the Zambia Population-Based HIV Impact Assessment (ZAMPHIA) 2016, the overall prevalence of syphilis in individuals aged 15 to 59 years is 3%. However, the prevalence is much higher in high-risk populations. A bio behavioral survey (BBS) was conducted among high risk populations in four cities in Zambia in 2021. In this survey, the prevalence of active syphilis among high risk ranged from 3.4% in one study site to 7.9%. There is limited data on the incidence of Chlamydia and Gonorrhoea; as they are not routinely tested for in demographic health surveys and in clinical settings. Zambia is currently using the syndromic approach in managing STIs. Genital discharge is one of the commonest STI syndromes. Some of the causes of genital discharge syndrome are *Chlamydia trachomatis* and *Neisseria gonorrhoea*.

1.3 Global Guidance for STI Prevention

In 2024, the Centres for Disease Control and Prevention (CDC) recommended the use of Doxycycline for the prevention of syphilis, chlamydia and gonorrhoea in high risk populations. This is commonly referred to as Doxy-PEP. This followed findings from 3 major randomized controlled trials that showed that Doxycycline when taken within 72 hours of unprotected sex was effective at reducing the risk of acquiring syphilis, chlamydia and to some extent gonorrhea (Bolan *et al.*, 2015; Molina *et al.*, 2018; Luetkemeyer *et al.*, 2023). In the first study, 330 high risk individuals who had a recent history of an STI were

randomized to receive Doxycycline or contingency management (CM). After 48 weeks of follow up, there were less frequent occurrences of syphilis, chlamydia or gonorrhoea among the Doxycycline group as compared to the CM group (odds ratio 0.27, 95% CI 0.09-0.83; $p=0.02$) (Bolan *et al.*, 2015). In a similar study, Molina *et al* randomized 232 high risk individuals to receive either Doxycycline within 24 hours of sex or no medication. There were 116 men in the Doxycycline group and 116 in the comparison group. After a follow up period of about 8.7 months, the incidence of STIs was lower in the Doxycycline group as compared to the comparison group (Hazard ratio 0.53, 95% CI 0.33-0.85; $p=0.008$) (Molina *et al.*, 2018). Luetkemeyer *et al* randomized high risk individuals who were either taking PrEP or People Living with HIV (PLWHIV) to take either Doxycycline or standard care. Participants had reported an STI in the preceding year. Participants in the Doxycycline group took 200mg of Doxycycline within 72 hours of unprotected sex. This study also showed a lower incidence of STIs in the Doxycycline group. Among the PrEP clients, the relative risk of an STI was 0.34 (95% CI 0.24-0.46; $p<0.001$). Among PLWHIV, the relative risk of an STI was 0.38 (95% CI 0.24-0.60).

At present, there is no evidence to recommend the use of Doxy-PEP among heterosexual men and women. There are few studies done in heterosexual women. An open-label randomized trial was conducted in Kenya, Africa, from 2020 and 2022, enrolling 449 cisgender, heterosexual women. Participants assigned to the intervention group received 200mg of Doxycycline within 72 hours of unprotected sexual intercourse. The study could not evaluate the effectiveness of Doxy-PEP in preventing syphilis, as only two cases of syphilis were identified during the study period. Further, Doxy-PEP was not effective in reducing the incidence of chlamydia (RR: 0.73; 95% CI 0.47-1.13) or gonorrhoea (RR: 1.64; 95% CI= 0.78-3.47). From this study, self-reported adherence to Doxycycline in weekly surveys was 78%. However, hair studies suggest that adherence to Doxycycline was much lower; as Doxycycline was detected in hair samples of only 29% of study participants. The evidence regarding the use of Doxy-PEP is summarized in table 1 below:

Table 1: Studies Evaluating the Efficacy of Doxy-PEP for Prevention of STIs

Study	Design	Participants	Intervention	Primary end point	Findings
Iprex Trial France 2018	RCT	232 high risk individuals on PrEP (TDF/FTC)	Doxycycline 200mg within 24 to 72 hours after unprotected oral or anal sex versus no intervention	First STI episode (chlamydia, gonorrhoea or syphilis) after 10 month follow up	Reduced risk of acquiring chlamydia (70%) and syphilis (73%). No effect on gonorrhoea
Doxy-PEP study USA, 2023	RCT	554 (N=360 on PrEP, 194 HIV+)	Doxycycline 200mg within 24 to 72 hours after unprotected oral or anal sex versus no intervention	Relative risk of an STI infection per quarter	PrEP: 65 STI end points (29.5%) in controls vs. 47 in Doxy-PEP group (RR 0.33, p=0.001), HIV+: 30 STI end points (27.8%) in controls and 31 (11.7%) in Doxy-PEP (RR=0.42, p=0.0014)
DoxyVac France, 2023	RCT	502 high risk individuals on PrEP	Doxycycline 200mg within 24 to 72 hours after unprotected oral or anal sex versus no PEP versus 4CMen B vaccine vs no vaccine	Impact of Doxycycline as PEP on time to first STI episode (Chlamydia, gonorrhoea or syphilis) and impact of 4CMen B vaccine on first episode of gonorrhoea	Reduced chlamydia, gonorrhoea and syphilis (aHR of 0.49, 0.1 and 0.21 respectively). 4CMenB vaccine was reduced incidence of gonorrhoea (aHR 0.49).
dPEP Kenya, 2023	RCT	N=449 cisgender women	Doxycycline 200mg within 24 to 72 hours after unprotected oral or anal sex versus no PEP	Any incident Chlamydia, gonorrhoea or syphilis	C. Trachomatis RR 0.73, 95%CI 0.47-1.13; N. Gonorrhoea RR 1.64 95% CI 0.78-3.47. Syphilis could not be assessed

1.4 Status of Doxy-PEP Implementation Globally

Doxy-PEP has been implemented in the United States of America. The United Kingdom and Europe have released guidance on Doxy-PEP implementation though approaches have been different. There is a general consensus that Doxy-PEP, when combined with other biomedical structural and behavioural interventions can have a meaningful impact on the prevention of STIs. South Africa also has a position paper on Doxy-PEP implementation. It is unclear whether some countries in Sub-Saharan African have implemented Doxy-PEP.

1.5 Safety Profile of Doxy-PEP

Doxycycline was well tolerated in the all the Doxy-PEP studies (Bolan *et al.*, 2015; Molina *et al.*, 2018; Luetkemeyer *et al.*, 2023; Chan *et al.*, 2023). Only 1.5% of study participants discontinued Doxycycline due to side effects. However, Doxycycline may cause hepatotoxicity. This may occur 1 or two weeks after commencing treatment. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome has been reported with

Doxycycline use (Mailhol *et al.*, 2010). DRESS syndrome usually presents 2 to 8 weeks after commencement of the drug. Features of DRESS syndrome include rash (which may be urticarial, vesicular, maculopapular, pustular, bullous, with cheilitis, erythroderma and target lesions), fever, abdominal pain, eosinophilia, leucocytosis and abnormal liver function tests. In severe cases, myocarditis, hepatitis, nephritis, pericarditis and colitis may occur. In severe cases and where hepatotoxicity is suspected, collect blood for liver function test and discontinue Doxycycline. Administer steroids and monitor ALT. Admit patient and monitor liver function. Offer supportive treatment with fluids, glucose monitoring, monitoring of coagulation (Choudary *et al.*, 2013).

1.5.1 Drug Interactions

There are several drugs that have been shown to interact with Doxycycline. They include the following:

- ✓ Isotretinoin
- ✓ Penicillin
- ✓ Antacids containing Magnesium, Calcium or Aluminium
- ✓ Iron
- ✓ Phenobarbital
- ✓ Phenytoin
- ✓ Warfarin
- ✓ Carbamazepine
- ✓ Digoxin

Antacids containing Magnesium, Aluminium or Calcium, Iron or Calcium supplements, and laxatives containing Magnesium may reduce absorption of Doxycycline. Doxycycline should be taken 1 or 2 hours before, or 1 or 2 hours after taking antacids, Magnesium containing laxatives and Calcium supplements (Patel *et al.*, 2023).

1.6 Acceptability

A survey among 2046 gay, bisexual and non-binary individuals in Australia showed that there was a high (75.8%) acceptability of Doxy-PEP (Holt *et al.*, 2025). Other studies have found high acceptability of Doxy-PEP (Demant *et al.*, 2024). In the study of Fredericksen *et al.*, study participants reported having peace of mind as they were not anxious about acquiring STIs while on Doxy-PEP (Fredericksen *et al.*, 2024).

1.7 Advantages and Disadvantages of Doxy-PEP

Available studies have shown that Doxycycline is effective in preventing acquisition of chlamydia, gonorrhoea and syphilis. However, there are some concerns about Doxycycline use for PEP. The advantages and disadvantages of Doxy-PEP are highlighted in the table 2 below:

Table 2: Advantages and Disadvantages of Doxy-PEP

Advantages	Disadvantages
Relatively cheap drug	Limited efficacy in cisgender women
Readily available even at rural health posts	Possibility of antimicrobial resistance (AMR) to tetracyclines
Only one 200mg dose required in a 24-hour period	Adverse effects such as nausea, vomiting, abdominal pain, gastric irritation, esophageal irritation, sunburn, predisposes to vulvo-vaginal candidiasis
Can be taken even daily for several months	Unclear whether effect on gonorrhoea is sustained
reduction in the stigma and anxiety associated with having an STI or exposing partners to STIs	Doxy PEP has the potential to cause micro biome shifts that can lead to chronic illnesses
Effective against chlamydia, syphilis and gonorrhoea	Unclear whether Doxy-PEP will have significant impact on cases of complicated syphilis
Doxy-PEP can be co-prescribed with PrEP	
Doxy-PEP has the potential to reduce STI incidence at population level	

2.0 Situation Analysis

An overview of the current situation as it applies to implementation of Doxy-PEP is shown in the table 3 below:

Table 3: Situation Analysis for Doxy-PEP Implementation

Category	Strengths	Barriers and Gaps
Planning and budgeting	• Doxycycline already included in the quantification of essential medications	• Doxycycline was not quantified for use as Doxy-PEP
Supply chain management	• Existing supply chain systems are adequate for maintaining adequate stocks	• Need to create separate system for tracking Doxycycline for PEP
Delivery platforms	• Existing PrEP and STI service delivery platforms can be used to deliver Doxy-PEP	• There is need for capacity building for all health-workers
Uptake and effective use	• Doxycycline already being used for STI treatment	• Lack of information about acceptability and uptake of Doxy-PEP for STI prevention
Monitoring, evaluation, and learning	• Existing DHIS2 tracker can be used for tracking Doxy-PEP	• Paper based M & E forms have to be developed

2.1 District Readiness Assessment: Assess Readiness for Doxy-PEP Implementation

There has been no engagement of key stakeholders at the districts. We have planned a district stakeholder meeting that will highlight the benefits of Doxy-PEP and prepare the selected facilities for implementation. This stakeholder meeting is crucial for engaging the key stakeholders and addressing barriers to implementation.

2.2 Facility Readiness Assessment

Facilities that are providing STI and PrEP services are considered ready to implement Doxy-PEP.

2.3 Roll-out Plans and Targets for Doxy-PEP

It is anticipated that at least 80% of the eligible high risk individuals will be enrolled onto Doxy-PEP within the first 6 months.

2.4 Private Health Sector Landscape

The initial Doxy-PEP roll out is planned for public facilities. After the evaluation of implementation in public facilities, Doxy-PEP may be rolled out to selected private health facilities.

3.0 Implementation Framework for Doxy-PEP in Zambia

3.1 Purpose

To guide clinicians on Doxy-PEP implementation as part of the comprehensive package for STI prevention.

3.2 Vision

To end the epidemic of sexually transmitted infections in Zambia by 2030 by using Doxy-PEP to prevent the acquisition of chlamydia, gonorrhoea and syphilis.

3.3 Goals

To assess feasibility, acceptability, uptake, and patterns of use of Doxy-PEP among HIV negative and HIV positive high risk individuals.

3.4 Implementation Objectives

1. To establish the feasibility, and acceptability of Doxy-PEP implementation in Zambia
2. To identify barriers and facilitators to implementation

3.5 Guiding Principles

1. **Partnerships:** We will establish strong partnerships with community leaders, CBOs, CSOs, health workers and researchers to facilitate the successful implementation of Doxy-PEP
2. **Leadership:** We will ensure appropriate, visionary, efficient and effective leadership at all levels during the implementation and roll out of Doxy-PEP
3. **Transparency and Accountability:** To ensure the highest standards of transparency in the roll out of Doxy-PEP, an accountability framework will be developed

4. **Human Rights-Based:** We will ensure Doxy-PEP is provided within the context of comprehensive sexual health services
5. **Affordability:** Doxy-PEP will be provided free of charge to eligible adults
6. **Cost-effectiveness:** A cost effectiveness analysis will be done during implementation to determine the cost-effectiveness of Doxy-PEP in reducing STIs
7. **Gender Responsive/Sensitivity:** As there is limited evidence to support the use of Doxy-PEP in women, this implementation plan is currently limited to high risk individuals
8. **Evidence-Based:** We will utilize lessons learnt from oral PrEP and CAB-LA implementation to guide Doxy-PEP implementation and scale up. Implementation research will be carried out to identify facilitators and barriers
9. **Equality and non-discrimination:** We will address the stigma and discrimination that limit utilization of Doxy-PEP and other sexual health services

Implementation Sites

Implementation will be in a phased approach. We will initially focus on the following facilities:

- UTH-Adult Infectious Disease Centre
- UTH Dermato-venerology Clinic
- All the GF supported High Risk Clinics in 13 districts

Table 4: Implementation Sites for Doxy-PEP

District	Facilities
Nakonde	Katozi Health Post, Nakonde Urban Health Centre
Mpulungu	Mpulungu District Hospital
Luangwa	Luangwa District Hospital, Luangwa Boma Urban Health Centre
Kazungula	Kazungula District Hospital, Kazungula Wellness Centre Kazungula Rural Health Centre
Livingstone	Maramba Urban Clinic, Mahatma Gandhi Urban Clinic
Mansa	Mansa General Hospital
Kasama	Chisanga Urban Clinic, Kasama General Hospital
Chililabombwe	Kakoso Urban Clinic, Lubengele Health Post
Chipata	Kapata Urban Clinic, Muchini Health Post
Solwezi	Kazomba Health Post, Solwezi Urban Clinic
Kapiri	Kapiri Urban Clinic
Mongu	Lewanika General Hospital, Mongu District Hospital
Lusaka	University Teaching Hospital

3.6 Implementation Approach

The current recommendation is for Doxy-PEP to be given only to high risk men. There is no evidence to support the use of Doxy-PEP in women.

3.7 Eligibility Criteria

The following criteria will be used to commence Doxy-PEP in high risk men:

- High risk men with syphilis, gonorrhoea or chlamydia in the past year (where testing for chlamydia is available).
- High risk men with genital ulcer syndrome or urethral discharge syndrome.
- High risk men with a high likelihood for acquisition of a bacterial STI (e.g. multiple sex partners, HIV infection, low condom use)

3.8 How to Prescribe Doxy-PEP

Doxycycline (any form) 200mg orally x1, taken ideally ≤ 24 hours but no later than 72 hours after exposure. Patient should not exceed 200mg in a 24-hour period.

3.9 Pharmacokinetics and Pharmacodynamics of Doxycycline

Doxycycline is a bacteriostatic antibiotic that is used in a wide range of clinical conditions. It is used for treating infections caused by gram positive and gram negative bacteria. Some of the conditions in which Doxycycline is indicated include chlamydia, pelvic inflammatory disease, Lyme disease, rickettsia, typhus, tulareamia, cholera and mycoplasma (Patel *et al.*, 2023). Doxycycline is also used in a wide range of dermatological conditions such as acne vulgaris, rosacea, bullous dermatitis and vasculitis. It also has significant anti-malarial effects (Oakley, 2021).

Doxycycline exerts its effects by inhibiting protein synthesis. It binds to the 30s ribosomal subunit inhibiting protein synthesis. Bioavailability of Doxycycline in tissues is high as it is lipid soluble. Doxycycline is absorbed rapidly after oral administration and becomes detectable in the blood stream within 15 to 30 minutes. Peak plasma concentration is reached within 2 to 3 hours. The elimination half-life is 15 to 30 hours. Doxycycline is metabolised principally in the duodenum. Elimination is also mainly through the gastrointestinal tract. About 30 to 40% of the drug is excreted renally (Patel *et al.*, 2023).

3.10 Adverse effects of Doxycycline

- Photosensitivity
- Gastric irritation
- esophageal injury
- drug-drug interactions,
- contraindicated in pregnancy

Table 5: Strategies to Prevent/Minimize Adverse Reactions

Adverse Effect	Mitigation Strategies
Photosensitivity	Avoid excessive sun exposure while on Doxycycline. Use a sunscreen with Sun protective factor SPF 30 or above where available
Esophageal injury	Do not lie down immediately after taking Doxycycline. Wait at least an hour. Take with a lot of fluid and after meals
Drug-drug interactions	Inform your doctor of all medications you are taking. Do not take Doxy-PEP if you are taking medication that can interact with it

3.11 Differentiated Service Delivery (DSD) for Doxy-PEP

Multi-month dispensation that coincides with PrEP or ART clinic refills is recommended. Initial supply should be for one month. Follow up with client to assess use of Doxy-PEP and any side effects. After the 1st month review, supply adequate doses for 30 days.

3.12 Monitoring Patients on Doxy-PEP

3.12.1 Clinical Monitoring

Screen for STIs at each visit using syndromic guidelines. Ask about the following symptoms:

- Urethral discharge
- Rectal discharge/discomfort/bleeding
- Genital ulcers
- Rashes on the private areas
- Swellings in the scrotum
- Swellings in the groin

Ask about use of Doxy-PEP, how many doses taken since last visit. Enquire about side effects.

3.12.2 Laboratory Monitoring

- HIV testing every 3 months
- RPR test every 3 months
- Hepatitis B test at Baseline and whenever available
- Hepatitis C testing where available

3.12.3 Referral and Linkages

- Refer for other services such as VMMC, PrEP, PEP, mental health support, immunization
- Risk reduction counselling at each visit

3.12.4 Other Considerations for Implementation

- Prioritize STI screening in all ART clinics, mobile and fixed PrEP delivery sites, youth friendly spaces and wellness spaces
- STI screening to be done at every visit
- Provide condoms to all clients as part of combination prevention
- Ensure clients are given adequate information about STI prevention, HIV testing, side effects of Doxycycline

3.13 Managing new STIs in Patients on Doxy-PEP

- Treat new STIs according to Zambia STI treatment guidelines
- If exposed to early syphilis within prior 90 days, test and treat empirically regardless of Doxy-PEP use
- For any other high-risk exposure, treat according to the STI syndrome they have been exposed to or diagnosed with

Table 6: Expected Doxy-PEP Outcomes

Eligibility	• Number of high risk clients who are screened and found to be eligible for Doxy-PEP • Number ineligible individuals and reasons why
Uptake	Number of eligible clients who commence Doxy-PEP
Persistence	Number of clients who start Doxy-PEP who return to clinic for drug pick up at month 1, month 3, month 6, month 9 and month 12
Fidelity	Proportion of high risk clients who are prescribed Doxy-PEP according to the recommended guidelines
Acceptability	• How comfortable are you with Doxycycline tablets? • How much effort did it take on your part to take Doxy-PEP? • How much do you think Doxy-PEP has protected you from getting STIs? • How well do you think taking Doxy-PEP will work to prevent STIs? • How confident do you feel in your ability to use Doxy-PEP as prescribed by your healthcare provider?
Tolerability	Number of clients who discontinue Doxy-PEP due to side effects, dislike of going to the clinic
Discontinuation	Number of clients who are lost-to-follow-up or discontinue (include reasons for discontinuation)
Adverse Events	Gastric irritation, esophageal irritation
Incident STIs	Number of clients diagnosed with urethral discharge, genital ulcer syndromes while on Doxy-PEP Number of clients who test positive for syphilis (using RPR tests, RST test with or without TPHA)
STI risk at each visit	Self-perception of STI risk
Services delivery models	Health Facility based, pharmacy based, community based, other DSD models
Independent variables	Age, sex, education, etc.

4.0 Essential Health Systems for Implementation

4.1 Governance and Coordination

Leadership and oversight for Doxy-PEP implementation will be provided by the Director of Infectious Diseases with the support of the infectious diseases team. Monitoring of the implementation will be done by the National STI coordinator and the GF prevention team.

4.2 Demand Generation for Doxy-PEP

- The following are some of the approaches that will be used to create demand for Doxy-PEP
- Targeted messaging about the benefits of Doxy-PEP in high STI transmission settings
- Provision of IEC materials on Doxy-PEP to high risk individuals as they receive services at various service delivery points
- Initial demand generation will be at facility level and sub-national level in the implementing districts
- Address myths and misconceptions about STIs and Doxy-PEP use
- Pilot testing of messages with Social and Behavior Change Communication (SBCC) Technical Working Group (TWG)
- Use of Social media platforms visited by high risk individuals to disseminate key Doxy-PEP messages
- Peer to Peer messaging by high risk clients within their social networks
- Combination approaches are most likely to be effective in reaching wider audiences

4.3 Medicines and Medical Supplies

Doxycycline is one of the drugs on the essential medicines list. However, the use of Doxy-PEP will require the purchase of larger quantities of the drug, as the drug will be taken more frequently than before. There is need to engage ZAMMSA prior to implementation to ensure that more stocks of Doxycycline are procured and stocked at implementation sites.

Table 7: Commodities and Supplies

Doxycycline	100mg tablets
HIV Test Kits	Determine HIV test
	Bio line HIV test
	HIV self-tests
Test Kits for STIs and HBV	HBsAg, RPR,TPHA

4.4 Financing of Doxy-PEP

It is anticipated that the Ministry of Health will provide the resources that are required for purchasing Doxy-PEP in order to ensure commodity security and sustainability. We will reach out to stakeholders (CHAI, WHO, Evidence Action) for additional support for the development of IEC materials, finalization of implementation plan and for capacity building of health workers.

4.5 Service Delivery

Doxy-PEP will be offered to clients accessing STI screening, HIV testing and HIV prevention and treatment services at the facilities listed above. Clinicians that have been oriented in Doxy-PEP implementation will lead the implementation. Service delivery will be part of comprehensive STI prevention. Risk reduction counselling, HIV testing, PrEP, condoms and lubricants will be provided. A summary of the comprehensive services to be provided to clients accessing Doxy-PEP is given in the table below:

Table 8: WHO Recommended Optimal STI Services

Service	Focus areas	Responsible HCW
Information	• Modes of transmission and cure • Prevention • Self-recognition of signs and symptoms • Places to seek care. • Partner notification	STI/PrEP unit in charge, nurses, clinicians
Counselling	• Information sharing • Support for vaccination, testing, treatment, completion and linkage to care • Assist with partner notification • Prompting for STI symptoms and signs at each clinical interaction • Counselling on choices and modes of action of various HIV prevention options • Risk reduction counselling • Pre-HIV test counselling • Contraceptive options	Trained counsellors, STI/PrEP unit in charge, nurses, clinicians
Prevention	• Provision of combination HIV prevention that provides condoms in addition to any other biomedical prevention option. • Female condoms • Male condoms • Lubricants • Vaccination for Hep A, B, and HPV • Doxy-PEP for high risk individuals	Nurses, clinicians (HNPs, COs, MOs)
Testing	• Rapid testing for syphilis and HIV using the dual test kit were available • Confirmatory testing for syphilis • Testing for chlamydia and Neisseria where available	Trained counsellors, facility-based volunteers, nurses,
Partner Services	• Offer options on how to notify sexual and needle sharing partners i.e., client-initiated notification and provider assisted notification	Clinicians, counsellors, Community health workers

Clinical consultation	• Ensure consultation room provides privacy • Obtain detailed sexual history • Perform clinical examination with focus on lymph nodes, buccal cavity, Genital and anal areas, detailed examination of the skin, including skin on the palms and the soles of the feet • Speculum examination and anoscopy where appropriate	Clinicians (HNPs, nurses, COs, ML, MOs)
Treatment and follow-up	• Use syndromic management to treat cases if lab testing (etiological diagnosis) is not available • Follow up patients with persistent symptoms and refer to higher level facility for testing, AMR • Assess for treatment failure (adherence, reinfection, AMR, other STIs)	Clinicians (HNPs, nurses, COs, ML, MOs)
Referrals and linkages	• Refer complicated cases to referral centres/ centres of excellence • Strengthen referral systems, ensuring same day linkage to care and feedback given to referring facility	Trained counsellors, community health workers, STI/PrEP unit in charge, nurses, clinicians

5.0 Site Readiness for Service Delivery

5.1 Human Resources

The Ministry of Health, with the support of stakeholders, will build capacity of healthcare providers for Doxy-PEP implementation.

5.1.1 Cadres

The initial implementation of Doxy-PEP will be done by medical officers, medical licentiates and clinical officers. However, training for Doxy-PEP will be extended to the pharmacy and laboratory.

5.1.2 Provider Training

Doxy-PEP training will be part of comprehensive STI training. This will include training in syndromic treatment guidelines, HIV prevention options, risk reduction counselling, monitoring adverse drug reactions and monitoring and implementation.

5.1.3 Mentorship/Supervision

Quarterly mentorship and supervision will be done throughout implementation

5.2 Data Collection and Management

Clinical data will be captured using the initial eligibility assessment form, continuation form and discontinuation forms. These have been adapted from the forms used for PrEP implementation. Data collection tools are attached as appendices 1 and 2.

5.3 Pharmacovigilance, Safety and Monitoring

Active pharmacovigilance will be done using existing tools that were developed by Zambia Medicine Regulatory Authority (ZAMRA) National Pharmacovigilance Unit (NPVU). Clinicians will be trained on common adverse effects of Doxycycline and how to document and report them.

6.0 Monitoring, Evaluation and Learning

6.1 Introduction

This section outlines the Monitoring and Evaluation (M&E) framework for assessing the uptake, accessibility, effectiveness, and overall impact of the Doxy-PEP program. The M&E sections will outline the methods of data collection that will be used to collect data for Doxy-PEP.

6.2 Data Collection Methods

To effectively monitor and evaluate the performance of the Doxy-PEP program, it is essential to collect data that measures progress. Data collection will be done through the routine data collection systems and the use of surveys.

6.3 Routine Data Collection

The primary data sources for Doxy-PEP provision will include the Doxy-PEP Screening Form and the Doxy Clinical Form. The Doxy-PEP data will be collected using either electronic or paper-based systems. In facilities with the capacity to utilize both methods, the electronic system should be preferred over the paper-based system.

6.4 Paper-Based System

For the paper-based approach, facilities will maintain hard copies of the Doxy-PEP eligibility and clinical follow-up visit forms. After forms are completed, clinicians or data clerks are expected to update the Doxy-PEP register. This register collects essential data elements for reporting purposes. The data elected in the Doxy-PEP register will also be used to update the Health Information Aggregation (HIA) forms, which are subsequently integrated into the District Health Information Software (DHIS2).

6.5 Electronic System

In the electronic system, patient-level information will be entered into a digital format, stored within the DHIS tracker. The electronic system can be implemented in three modes: E-Last, E-Fast, or E-First.

1. **E-Last Mode:** Data is recorded after all clients have been seen. Information from paper records that is from Doxy-PEP eligibility and Clinical forms should be transferred into the DHIS2 tracker. The forms should update the patient level

information. Facilities must ensure that all client data is entered by the end of each month, with no backlog for reporting

2. **E-Fast Mode:** Similar to E-Last, but providers must ensure that the system is updated before the client leaves the facility
3. **E-First Mode:** This mode exclusively utilizes the electronic system (DHIS2 Tracker), where Doxy-PEP eligibility and clinical forms are integrated directly into the DHIS2 tracker

Once data is entered into the DHIS2 tracker, personal identifiers such as names and phone numbers will be de-identified to maintain confidentiality for official above the health facility. The summarized data will be incorporated into the HIA form and embedded into the DHIS2.

6.6 Surveys

To evaluate program effectiveness, surveys may be utilized. Existing surveys related to HIV/AIDS and STIs will be employed to assess the program's performance over a minimum evaluation period of four years.

Proposed indicators for tracking the progress of implementation and desired outcomes are listed in the table below:

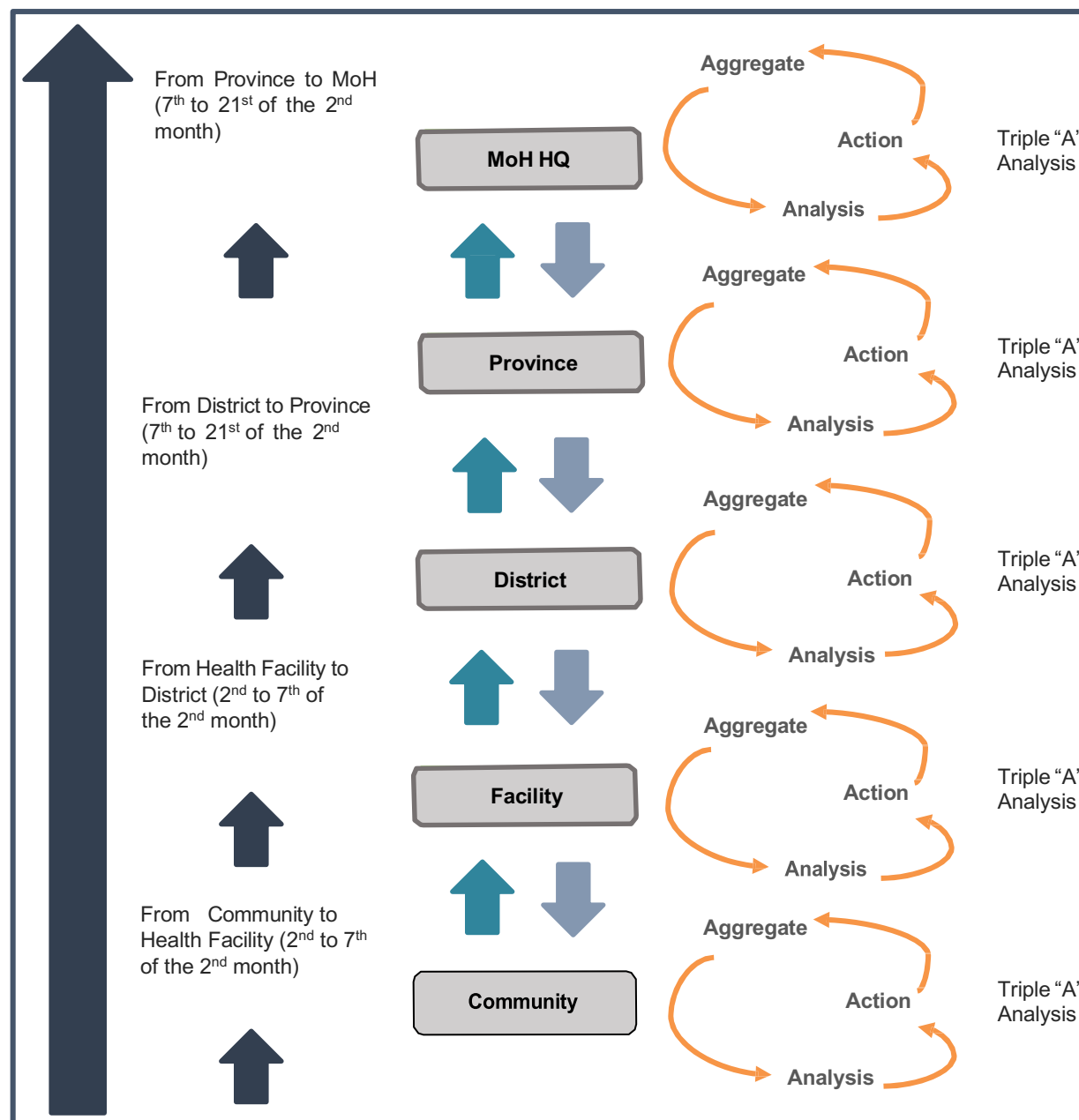
Table 9: Indicators for Tracking Doxy-PEP Implementation

Indicators	Numerator	Denominator	Disaggregation	Data Source	Reporting Frequency
Percentage of clients screened for eligibility for Doxy-PEP and found eligible for Doxy-PEP	Number of clients screened for Doxy-PEP eligibility and found eligible for Doxy-PEP	Number of clients screened for Doxy-PEP eligibility	Location, Population type, age, HIV status	Doxy-PEP Register/DHIS Tracker	Monthly
Percentage of clients who were eligible for Doxy-PEP and initiated Doxy-PEP	Number of clients who were eligible for Doxy-PEP and initiate Doxy-PEP	Number of clients who were eligible for Doxy-PEP	Location, Population type, age, HIV status	Doxy-PEP register/DHIS Tracker	Monthly
Percentage of clients continuing Doxy-PEP	Number of clients who are currently on Doxy-PEP	Number of clients who were started on Doxy-PEP at time x	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months)	Doxy-PEP register/DHIS Tracker	Monthly
Percentage of clients on Doxy-PEP reporting having adverse drug reaction (ADR)	Number of clients on Doxy-PEP reporting having adverse drug reaction (ADR)	Number of clients on Doxy-PEP	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months), severity	Doxy-PEP register/DHIS Tracker	Monthly
Percentage of clients on Doxy-PEP reporting having adverse drug event (ADE)	Number of clients on Doxy-PEP reporting having adverse drug event (ADE)	Number of clients on Doxy-PEP	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months), severity	Doxy-PEP register/DHIS Tracker	Monthly

Indicators	Numerator	Denominator	Disaggregation	Data Source	Reporting Frequency
Percentage of clients on Doxy-PEP who stopped due to adverse drug reactions	Number of clients who stopped Doxy-PEP due to adverse drug reaction	Number of clients who stopped Doxy-PEP	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months), ADE, ADR	Doxy-PEP Register/DHIS Tracker	Monthly
Percentage of clients on Doxy-PEP who report a new STI syndrome	Number of clients on Doxy-PEP who report a new STI syndrome	Number of clients on Doxy-PEP	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months)	Doxy-PEP Register/DHIS Tracker	Monthly
Percentage of clients on Doxy-PEP with a new STI syndrome and are started on treatment	Number of clients on Doxy-PEP with a new STI syndrome and are started on treatment	Number of clients on Doxy-PEP who report a new STI syndrome	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months)	Doxy-PEP Register/DHIS Tracker	Monthly
Percentage of clients on Doxy-PEP with a new STI syndrome whose partners were screened for STIs	Number of clients on Doxy-PEP with a new STI syndrome whose partners were screened for STIs	Number of clients on Doxy-PEP who had a new STI syndrome	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months)	Doxy-PEP Register/DHIS Tracker	Monthly
Percentage of partners of clients on Doxy-PEP who had new STI syndrome and were treated	Number of partners of clients on Doxy-PEP who had new STI syndrome and were treated	Number of partners of clients on Doxy-PEP who had a new STI syndrome	Location, Population type, age, HIV status (Timing 3, 6, 9 and 12 months)	Doxy-PEP Register/DHIS Tracker	Monthly

Below is the Data flow guideline from Community to National level

HMIS Data Flow Guidance



7.0 Monitoring for Doxycycline Resistance

There is a general concern that widespread implementation of Doxy-PEP will lead to antimicrobial resistance to tetracyclines (Chu *et al.*, 2025). Many gonococcal isolates are already resistant to tetracyclines (Do *et al.*, 2025). Consequently, Doxy-PEP has had variable effects on the incidence of gonorrhoea in clinical trials. However, it is important to note that Doxycycline is already being used for prophylaxis against malaria, Lyme disease and other spirocheate infections. Doxycycline has also been used for prolonged periods for treating acne (Patel *et al.*, 2023). Despite the concerns about possibility of drug resistance, there were no reports of resistance during the clinical trials. However, more research is required to evaluate the impact of Doxy-PEP roll out on resistance to tetracyclines and the disruption of the microbiome (Truong *et al.*, 2022). At present, there is little information about resistance to Tetracyclines in Zambia.

7.1 Mechanism of Resistance to Doxycycline

There are several mechanisms by which bacteria become resistant to Doxycycline:

- Acquisition of Tetracycline specific resistance genes
- Mutations in 30S ribosomal sub-unit binding site
- Intrinsic resistance induced by chromosomal mutations

The above factors can lead to resistance by causing efflux of Doxycycline out of the cell, ribosomal protection or inactivation of the drug by enzymatic action.

7.2 Criteria for Suspected Resistance

Patients presenting with persistent or recurrent urethral discharge following standard syndromic management treatment for urethral discharge that includes Doxycycline, should be prioritized for resistance testing (WHO, 2021)

Indicators of suspected resistance include:

- **Persistent Symptoms:** Symptoms that do not resolve after completing the full treatment course
- **Recurrent Episodes:** Multiple episodes of urethral discharge occurring within a brief timeframe
- **Treatment Failures:** Documented instances of treatment failure in the patient or their partners

7.3 Sample Collection Process

- Collect urethral swabs or first-catch urine samples before administering any further antibiotics (WHO, 2021)
- Ensure that samples are labelled accurately and packaged in leak-proof containers clearly marked as bio-hazardous
- Where possible, provide instructions for self-collection to enhance accessibility and safeguard privacy (WHO, 2021)

7.4 Courier System

Utilize an established courier network to transport samples to designated AMR sentinel laboratories. It is essential to adhere to cold chain protocols and maintain tracking systems to ensure timely delivery.

7.5 Laboratory Diagnosis

7.5.1. Phenotypic Method

This is achieved through Inoculation of urethral secretions on the selective medium, incubation of culture plates, Gram stain and biochemical reactions. Antimicrobial susceptibility testing (AST) by minimum inhibitory concentrations (MICs; $\mu\text{g/mL}$) of tetracycline would be determined by E-test with reference strains for results validity.

7.5.2. Genotypic Method

Molecular Point-of-care (POC) testing can rapidly detect *Neisseria gonorrhoea* and *Chlamydia trachomatis*, and, where applicable, identify genetic markers associated with tetracycline resistance. The Xpert CT/NG assays, which are compatible with both urethral swabs and urine samples, facilitate timely and accurate surveillance of resistance patterns.

Table 10: Key Steps in AMR Monitoring for Doxy-PEP

Step	Action	Rationale
Identify Suspected Cases	Persistent/recurrent symptoms after Doxycycline	Early detection of resistance
Collect Samples	Urethral swab or urine before further antibiotics	Enables accurate resistance testing
Transport Samples	Use courier system to AMR sentinel labs	Maintains sample integrity
Laboratory Testing	Use Xpert machines for rapid detection and resistance markers	Supports timely management
Update Protocols	Modify treatment guidelines based on resistance data	Maintains treatment efficacy

7.6 Research Recommendations

Continued research is essential to assess the impact of Doxy-PEP on Tetracycline resistance and to explore potential disruptions to the human microbiome.

7.7 Conclusion

Strategies for monitoring AMR to Doxycycline requires coordinated efforts across diagnostic, clinical, and public health domains. The implementation of structured resistance surveillance strategies, combined with advances in rapid diagnostic technologies like Xpert machines, represents a critical step towards preserving the efficacy of tetracyclines in the face of rising AMR challenges. Continued research and adaptation of management strategies will be essential to safeguard against the potential

repercussions of AMR, thereby ensuring the ongoing effectiveness of Doxycycline and similar treatments in managing urethral discharge and associated infections. As we move forward, enhancing collaboration among healthcare providers, laboratories, and policymakers will be paramount in tackling this pressing public health issue.

8.0 Ethical Considerations

There are concerns about long term benefits and the possibility of developing side effects and antimicrobial resistance with long term use. The actual duration for which Doxy-PEP can be used safely remains unclear. The benefits of Doxy-PEP need to be weighed against risks.

Doxy-PEP should only be given when client has been fully engaged in discussions about the risks and benefits and they are aware of the need to take repeated doses as long as risk persists.

There is also need to engage all the relevant stakeholders including the high-risk populations, ZAMMSA, pharmacists, provincial and district health teams, antimicrobial surveillance teams in order to maximize benefits and minimize potential harms. Finally, there is a need to ensure that implementation will be done in a way that ensures equity of access to all who are most likely to benefit.

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Appendices

Appendix 1: Proposed Timelines for Doxy-PEP

Task	2025							2026				
	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
Policy Environment												
Development of Doxy-PEP implementation Plan	X	X	X									
Stakeholder engagement meetings		X	X	X								
Submission of Doxy-PEP implementation plan				X								
Service Delivery												
Updating of STI training package and treatment Guidelines	X	X	X	X								
Development and dissemination of IEC materials				X	X	X	X					
Revising Data Collection Tools				X	X							
Secure additional Doxycycline for Doxy-PEP implementation					X	X	X	X	X	X	X	X
Human Resources												
Training of Healthcare Workers (Clinical, Laboratory, Pharmacy)				X	X	X	X	X				
Training of Demand Generation Teams							X	X	X	X		
Monitoring antimicrobial resistance												
Development of AMR tool for Doxycycline					X	X						
AMR training for lab and facility staff							X	X				
Data Analysis and Review									X	X	X	X

Appendix 2: Doxy-PEP Eligibility Assessment Form

DOXY-PEP ELIGIBILITY SCREENING FORM

This form is to be used to assess eligibility for Doxy-PEP among high risk individuals

CLIENT ID/NUPIN																
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Province:	
District:	Facility/Site Name:
Client Name:	Client Phone No.
Sex at birth: ☐ Male ☐ Female	Date of Birth (dd/mm/yyyy): ____ / ____ / ____
Population category:	Age:
Client Physical Address:	
Client NRC #:	
Date of last visit (dd/mm/yyyy): ____ / ____ / ____	Today's date (dd/mm/yyyy): ____ / ____ / ____
Visit type	☐ Eligibility assessment and initiation visit ☐ Restart

Physical Examination			
Temp:	BP:	Pulse:	Resp Rate:
Body Weight*:	Height:	Body Mass Index:	
Pallor: ☐ Yes ☐ No	Jaundice: ☐ Yes ☐ No	Hepatomegaly: ☐ Yes ☐ No	

Laboratory Examination		
Determine HIV test result: Date (dd/mm/yyyy): ____ / ____ / ____	RPR titres for patients with positive RPR Date (dd/mm/yyyy): ____ / ____ / ____	Creatinine Date (dd/mm/yyyy): ____ / ____ / ____
RPR test Results Date (dd/mm/yyyy): ____ / ____ / ____	TPHA test result: Date (dd/mm/yyyy): ____ / ____ / ____	ALT results: Date (dd/mm/yyyy): ____ / ____ / ____
HBsAg results : Date (dd/mm/yyyy): ____ / ____ / ____	HCV results: Date (dd/mm/yyyy): ____ / ____ / ____	

SN	Doxy-PEP Eligibility Assessment		
1. Status Neutral Approach: HIV Prevention or Treatment			
1.	Are you living with HIV?	☐ Yes ☐ No	If Yes, proceed to other next questions. If No, proceed to question 6
2.	Are you currently on ART?	☐ Yes ☐ No	If No
3.	If Yes, when did you start ART?	Date (dd/mm/yyyy): ____ / ____ / ____	
4.	Is your partner also on ART?	☐ Yes ☐ No	
5.	If No, to question 4, is your partner on PrEP?	☐ Yes ☐ No	If partner not on PrEP but eligible encourage to bring partner
6.	What type of HIV prevention methods are you using? ☐ CAB-LA ☐ Oral PrEP ☐ Condoms ☐ None	☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No	
7.	Have you used any other HIV prevention methods in the past?	☐ Yes ☐ No	
8.	If Yes, why did you stop? Select all that apply. ☐ Pill burden ☐ No longer at risk ☐ Negative response from partner / possible intimate partner violence ☐ Side effects ☐ Adverse reactions to oral PrEP ☐ Other	☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No	

9.	If still on, for how long have you used Oral PrEP or CAB LA?	☐ <3mths ☐ <6mths ☐ >6mths ☐ >12mths	
2. Sexual History and History of Sexually Transmitted Infections			
1	In the last 12 months, have you been treated for sexually transmitted infection?	☐ Yes ☐ No	Assess risk of STI
2	Has any of your sexual partners been treated for an STI?	☐ None ☐ Some	
3	Do you have sex with more than one sexual partner?	☐ Yes ☐ No	
3. Screening for Sexually transmitted infections			
1	Do you have abnormal urethral/vaginal discharge from your private parts?	☐ Yes ☐ No	Treat STI according to national guidelines
2	Do you have genital ulcers/sore(s) or a rash on your private parts?	☐ Yes ☐ No	
3	Do you have dysuria when passing urine?	☐ Yes ☐ No	
4	Do you have pain/discomfort in lower abdomen, buttocks, itching on private parts or lymph node swelling?	☐ Yes ☐ No	
4. Drug – Drug Interaction screening.			
1	Are you currently taking any of the medication listed below? 1.1.1. Isotretinoin 1.1.2. Penicillin 1.1.3. Antacids containing Magnesium, Calcium or Aluminium 1.1.4. Iron 1.1.5. Phenobarbital 1.1.6. Phenytoin 1.1.7. Warfarin 1.1.8. Carbamazepine 1.1.9. Digoxin	☐ Yes ☐ No	Action: Do not commence Doxy-PEP. Consult Infectious Diseases team
For clients taking			
5. Contraindications for Doxycycline			
Do you have any of the following conditions?		Response and Score	Grading
1	Peptic ulcer disease	☐ Yes = 1 ☐ No = 0	If a client has one or more contraindications, do not start Doxy-PEP
2	Esophagitis	☐ Yes = 1 ☐ No = 0	
3	Hypersensitivity to tetracyclines	☐ Yes = 1 ☐ No = 0	
4	Systemic Lupus Erythematosus	☐ Yes = 1 ☐ No = 0	
5	Antibiotic associated colitis		
6	Hemolytic anaemia		
7	Porphyria (blood disorder)		
8	Myasthenia Gravis		
9	Recurrent fungal infections		
6. Clinical Decision			

Is the client eligible for Doxy-PEP?		☐ Yes ☐ No
If yes, provide prescription for 30 days' supply of Doxycycline (60 tablets 100mg each) <i>Insert the dates (dd/mm/yyyy) ____ / ____ / ____</i>		
Next visit	☐ 30 Days	
Provider Name:		Sign:

Any other comments

Remember to discuss the importance of comprehensive prevention (use of condoms; contraception; risk reduction; VMMC) with each client.