Standard Operating Procedures on Provision of Pre-Exposure Prophylaxis (PrEP) for HIV Infection In Myanmar

2023

National AIDS Programme
Department of Public Health
Ministry of Health, Myanmar

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Contents

Acronyms

3TC	Lamivudine
ARV	Antiretroviral
CABLA	Long-acting injectable cabotegravir
CrCl	Creatinine Clearance
DVR	Dapivirine Vaginal Ring
FSW	Female Sex Worker
FTC	Emtricitabine
GPs	General Practitioners
HBsAg	Hepatitis B Surface Antigen
HIV	Human Immunodeficiency Virus
HIVST	HIV Self-Testing
KPSC	Key Population Service Centre
MMT	Methadone Maintenance Therapy
MSM	Men who have sex with men
NAP	National AIDS Programme
NGO	Non-Governmental Organization
NSP	Needle and Syringe Programme
PEP	Post-Exposure Prophylaxis
PrEP	Pre-Exposure Prophylaxis
PWID	People who inject drugs
SOP	Standard Operating Procedures
STI	Sexually Transmitted Infection
TDF	Tenofovir Disoproxil Fumarate
TG	Transgender
UN	United Nations

Acknowledgements

Myanmar's fourth National Strategic Plan for HIV/AIDS (2021-2025) (NSP-IV) has included Pre-Exposure Prophylaxis (PrEP) of HIV infection as one of the innovative prevention strategies to further strengthening of Myanmar's commitment to fast track the HIV response and to end the AIDS epidemic as a public health threat by 2030.

In light of this, a Standard Operation Procedures on the provision of Pre-Exposure Prophylaxis (PrEP) for HIV infection in Myanmar was developed in November 2019. This revised Standard Operation Procedure was developed in accordance with the updated global recommendations which tailored to the Myanmar context in consultation with concerned key stakeholders in the country.

The National AIDS Programme would like to express its acknowledgement to key stakeholders who contributed for development of this revised version of PrEP SOP.

Programme Manager

National AIDS Programme

Department of Public Health

Ministry of Health

Executive Summary

WHO recommends oral Pre-Exposure Prophylaxis (PrEP) containing Tenofovir Disoproxil Fumarate (TDF) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (strong recommendation, high quality evidence). PrEP is encompassed as one of the innovative prevention strategies in country's fourth National Strategic Plan for HIV/AIDS, 2021-2025 (NSP-IV) to further strengthening of Myanmar's commitment to fast track the HIV response and to end the AIDS epidemic as a public health threat by 2030.

This "Standard Operation Procedures on provision of Pre-Exposure Prophylaxis (PrEP) for HIV infection in Myanmar" is developed in accordance with the global recommendations which tailored to the Myanmar context in consultation with concerned key stakeholders in the country, including leading HIV clinicians, UN agencies and technical partners, implementing partners and community groups. This SOP was revised in 2023 to reflect the most updated global recommendations and contextualizing in to local context.

PrEP is the use of antiretroviral (ARV) drugs by people who do not have HIV infection in order to prevent the acquisition of HIV. This SOP recommends oral PrEP containing TDF as an additional prevention tool for people at substantial risk of HIV infection as part of the combination HIV prevention approaches with the drug of choice option of using either TDF/3TC or TDF/FTC. It provides information about how PrEP is safe and effective. Myanmar PrEP SOP embraces key technical information required for successful PrEP demonstration and implementation; eligibility criteria for PrEP including ruling out of HIV infection before PrEP initiation and assessing the substantial risks; procedures and services to be provided on initial and follow up visits including laboratory testing; monitoring and management of PrEP side effects and other special situations such as co-infection with Hepatitis B and C, Creatinine elevation, seroconversion, discontinuation of PrEP; key counselling messages about PrEP safety and effectiveness. The importance of community involvement and how to minimize the potential stigma around PrEP are also discussed. Algorithms and job aids are included to promote the users' friendliness to the SOP. In this revised SOP, NAP includes updated global guidance in accordance with local context after consultation with key stakeholders. Therefore, this SOP will serve as a technical reference to provide PrEP services in Myanmar as part of the combination prevention and build up additional momentum of National HIV response by reducing new infection.

I. PrEP Basics

1. What is PrEP?

Pre-Exposure Prophylaxis (PrEP) is the use of antiretroviral (ARV) drugs by people who do not have HIV infection in order to prevent the acquisition of HIV. Findings from several clinical trials have demonstrated that PrEP is effective in reducing the risk of acquiring HIV infection and safe in many different groups of people, including men and women in serodiscordant couples, men who have sex with men (MSM), transgender people, female sex workers, and people who inject drugs. The level of protection is high across different age, sex, regimen, and route of sexual acquisition of HIV. The level of protection was strongly correlated with adherence.

2. PrEP usage

WHO recommendations on PrEP for HIV prevention

- **2015:** Oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches *(strong recommendation, high certainty evidence)*
- **2021:** The DVR may be offered as an additional prevention choice for women at substantial risk of HIV infection as part of combination prevention approaches *(conditional recommendation, moderate-certainty evidence)*
- **2022:** Long-acting injectable cabotegravir (CABLA) may be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches *(conditional recommendation; moderate-certainty evidence)*

In Myanmar, oral PrEP containing tenofovir disoproxil fumarate (TDF) is recommended as an additional prevention tool for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

Starting, using and stopping Oral PrEP

WHO updated guidance includes dosing schedules for safely starting, continuing and stopping oral PrEP based on the gender and hormone use.

Table 1. How to safely start, use and stop TDF-based oral PrEP

	Population	Starting oral PrEP	Using oral PrEP	Stopping oral PrEP
A	Cisgender men and trans and gender diverse people assigned male at birth[a] who: • have sexual exposure AND • are not taking exogenous estradiol-based hormones	Take a double dose 2–24 hours before potential sexual exposure (ideally closer to 24 hours before potential exposure)	Take one dose per day	Take one dose per day until two days after the day of the last potential sexual exposure
B	Cisgender women and trans and gender diverse people assigned female at birth Cisgender men and trans and gender diverse people assigned male at birth who are taking exogenous estradiol-based hormones People using oral PrEP to prevent HIV acquisition from injecting practices	Take one dose daily for seven days before potential exposure	Take one dose per day	Take one dose daily for seven days after last potential exposure

[a] "Trans and gender diverse people" is an umbrella term for those whose gender identity, roles and expression does not conform to the norms and expectations traditionally associated with the sex assigned to them at birth; it includes people who are transsexual, transgender, or otherwise gender nonconforming or gender incongruent. Transgender people may self-identify as transgender, female, male, transwoman or transman, trans-sexual or one of many other gender nonconforming identities.

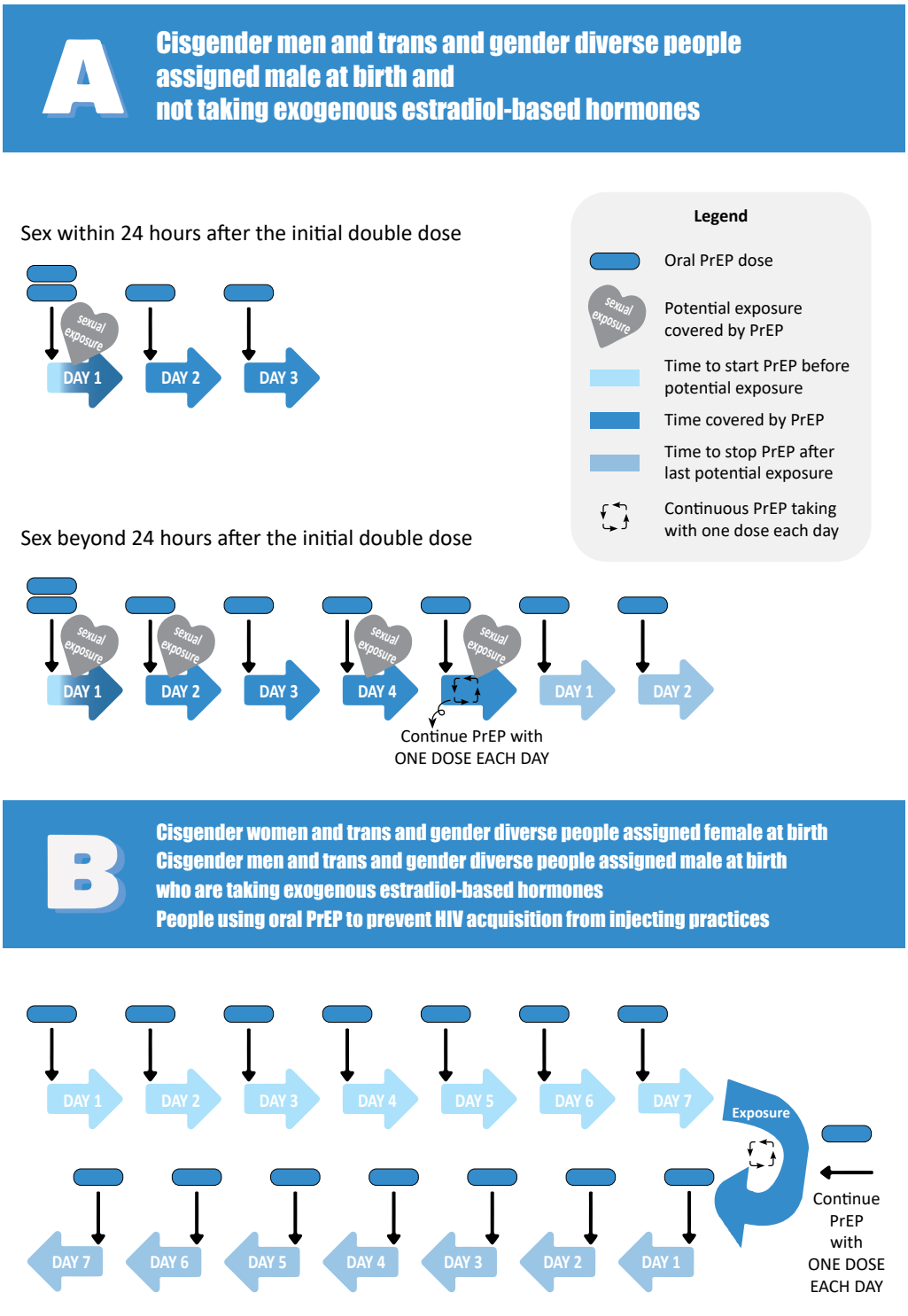


Figure 1. How to safely start, use and stop TDF-based oral PrEP

3. PrEP regimens containing TDF

TDF 300 mg/ 3TC 300 mg
(or)
TDF 300 mg/ FTC 200 mg

4. Safety of PrEP

PrEP is very safe. About 10% of people who start PrEP will have some short-term, mild side-effects. Side-effects may include gastrointestinal symptoms (diarrhoea, nausea, decreased appetite, abdominal cramping or flatulence). Dizziness or headaches have also been experienced. Such side-effects are usually mild and resolve without stopping PrEP. Typically, these symptoms start in the first few days or weeks of PrEP use and last a few days, and almost always less than one month. Serious side-effects are rare but can affect the kidney, liver and bone (slight decreases in bone mineral density)[1].

1 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Recommendation for a Public Health Approach, Geneva: World Health Organization, 2016

II. Eligibility of PrEP

1. Eligibility criteria for PrEP

Any individual must meet all the following criteria to be eligible for PrEP:

- HIV-negative
- no suspicion of acute HIV infection
- substantial risk of HIV infection
- Creatinine Clearance (CrCl) is more than 50 ml/min
- willingness to adhere PrEP as prescribed, including periodic HIV testing.

Please see Annex 2 for the "Tool for screening of substantial risk and eligibility for PrEP".

i. Ruling out of HIV infection before starting PrEP: HIV Testing and Acute HIV Infection

HIV Testing

PrEP is a prevention intervention for people who are HIV negative. Existing HIV infection should be ruled out by HIV testing. HIV testing must be performed according to the National HIV Testing Algorithm. Following figure shows the testing algorithm for HIV screening.

All specimens are tested with a highly sensitive assay (A1). Any person with non-reactive (A1-) result is considered HIV-negative. If there is no history or signs or symptoms of an acute viral syndrome, the person can be offered and initiated on PrEP.

A single reactive (positive) test result is not sufficient to make an HIV-positive diagnosis. If the initial serology test result is reactive (A1+), additional testing is needed to confirm an HIV- positive diagnosis according to National HIV Testing Algorithm for HIV confirmation (Annex 3). PrEP should not be prescribed in such cases.

HIV Self Testing (HIVST) using **WHO pre-qualified blood-based HIVST kit** can be considered as an additional testing option for PrEP users.

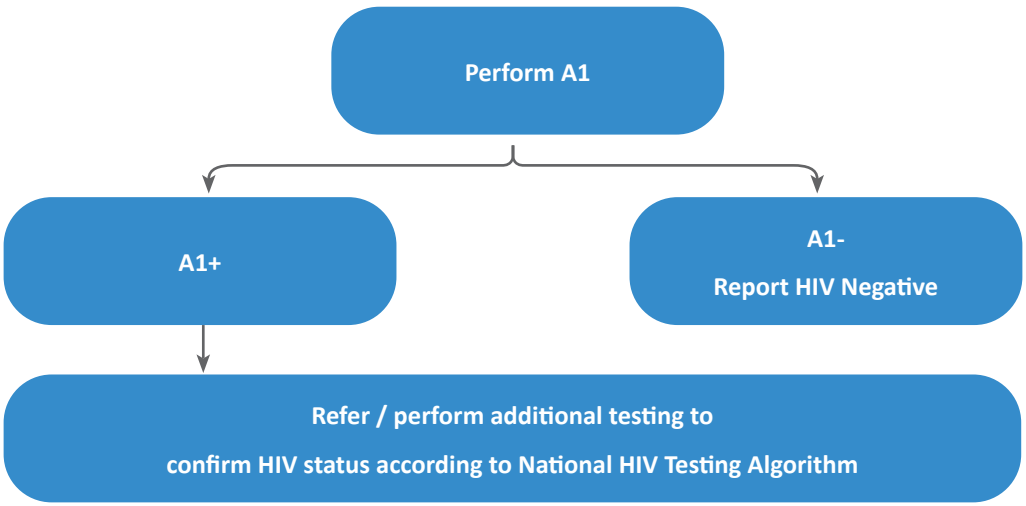
Clear and concise messages for HIVST use in PrEP initiation or continuation are critical.

- For initiation, following a reactive HIVST, individuals should not initiate PrEP and seek further testing by a trained provider.
- For continuation, following a reactive HIVST, PrEP users should not discontinue PrEP and immediately seek further testing by a trained provider.

WHO pre-qualified blood-based HIVST kit (as of December 2022)[2]

1. INSTI HIV self-test kit
2. Mylan HIV self-test kit
3. SURE CHECK HIV self-test kit
4. CheckNOW HIV self-test kit
5. Wondfo HIV self-test kit

Testing algorithm for HIV screening



A1 = Alere Determine HIV-1/2 (manufactured by Alere Medical Co., Ltd., Japan) (D) ICT (sensitivity 100% and specificity 99.75%) is recommended. If not available, WHO pre-qualified RDT with sensitivity and specificity similar to Determine.

Figure 2. Testing algorithm for HIV Screening

2 Prequalified in vitro diagnostics products, WHO at https://extranet.who.int/pqweb/vitro-diagnostics/vitro-diagnostics-lists accessed in Dec 2022

Acute HIV Infection

If there are signs or symptoms of an acute viral syndrome, including a flu-like illness such as fever, sore throat, aches and pains, lymphadenopathy (swollen glands), mouth sores, headache or rash, the possibility that acute HIV infection could be the cause should be considered. Therefore, for any person presenting with these signs and symptoms AND reporting recent exposure to HIV in the past 4 weeks, defer PrEP for 4-6 weeks and having the person tested for HIV again. This allows time for possible seroconversion to be detected. However, for those presenting with signs and symptoms of viral syndrome but having no recent exposure to HIV in the past 4 weeks, PrEP may be considered but an additional HIV testing should be done at 2-month after starting PrEP.

ii. Screening for substantial risk of HIV infection

PrEP should be considered for people who are at substantial risk of acquiring HIV. Clients who fall under one of the following 4 categories are assumed to have substantial risk.

I. Sexually active in a high HIV incidence/ prevalence population[3] **AND any of the following** in the last 6 months:
   - Vaginal or anal sexual intercourse without condoms with more than one partner, OR
   - A sexual partner with one or more HIV risk factors, OR
   - A history of a sexually transmitted infection (STI) by lab testing or self-report or syndromic STI treatment, OR
   - Use of post-exposure prophylaxis (PEP) for sexual exposure

II. People who inject drugs (PWID)*

III. The sexual partner of someone with HIV who is not on suppressive ART

IV. Individual requesting PrEP**

** WHO recommends PrEP as an additional prevention choice in a comprehensive package of harm reduction interventions.*

*** Individual risk varies considerably within populations depending on individual behaviour and the characteristics of sexual partners. In locations with a low overall incidence of HIV infection, there may be individuals at substantial risk who should be offered PrEP services.*

Individuals requesting PrEP should be given priority to be offered PrEP, since requesting PrEP likely indicates there is a risk of acquiring HIV.

3 Population in which HIV incidence/ prevalence is higher than national HIV incidence/prevalence among adult, such as key populations – FSW, MSM, TG and PWID

iii. Creatinine and Estimated Creatinine Clearance

The use of PrEP containing TDF is associated in some people with a small decrease in estimated creatinine clearance. This decrease does not usually progress during PrEP use and generally reverses after stopping PrEP.

Therefore, draw the blood for serum creatinine testing before PrEP initiation. PrEP can be initiated without waiting for the creatinine result. Stop PrEP if baseline CrCl is < 50ml/min. Before stopping oral PrEP due to reduced kidney function, the kidney function test should be repeated on another day.

Table 2. Measurement of serum creatinine at PrEP facilities

Population	Measurement of kidney function:	
	At initiation	At follow-up
Individuals under 30 years without kidney-related comorbidities	• can be screened within 1–3 months after oral PrEP initiation	• If initiation test result suggests at least mild loss of kidney function, follow-up measurements every 6–12 months are suggested
Individuals 30 years and older and those younger than 30 years who have comorbidities	• should be screened as baseline	• Follow up measurement 6 monthly

[a] Kidney-related comorbidities include chronic kidney disease or risk factors such as diabetes or hypertension. There may be an increased risk of kidney-related adverse events during pregnancy, and conditions such as preeclampsia may cause kidney impairment, so more frequent kidney function testing may be considered during pregnancy.

Creatinine Clearance can be calculated by using Cockcroft-Gault formula.

$$\text{Estimated CrCl} = \frac{\text{Sex} * (140 - \text{Age}) * \text{Weight}}{\text{Serum Creatinine} * 72}$$

Notes:

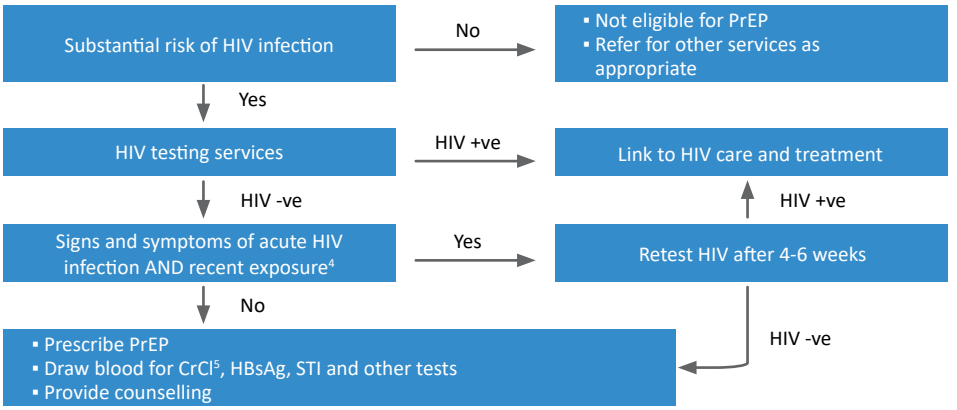
- For “Sex”, use 1 for a male, 0.85 for a female
- Give “Age” in years
- Provide “Serum Creatinine” in mg/dL
- Give “Weight” in kilograms

III. Initial and Follow Up PrEP Visits

1. Initial visit

Screening for substantial risks of HIV infection, confirmation of HIV-negative antibody status and clinical assessment for signs and symptoms of Acute HIV Infection should be done before PrEP is started. Explain the clients how PrEP works and the potential side effects of TDF-containing PrEP. Provide/ Link with other combination prevention services including condoms, lubricants, and harm reduction services such as Needle and Syringe Programme (NSP), Methadone Maintenance Therapy (MMT) etc. for PWID population as appropriate. The following flow chart summarizes the procedures suggested to be undertaken for PrEP initiation

Flow Chart for PrEP initiation



Note: PrEP can be provided on the same day that a client presents to the service under the following conditions:

- HIV testing has been performed and the client found to be HIV negative
- There are no signs or symptoms of acute HIV infection and no recent exposure
- Behavioural eligibility has been assessed

Specimens for other laboratory tests have been collected and the client can be contacted if test results require additional action, confirmation or treatment.

Figure 3. Flowchart for PrEP initiation

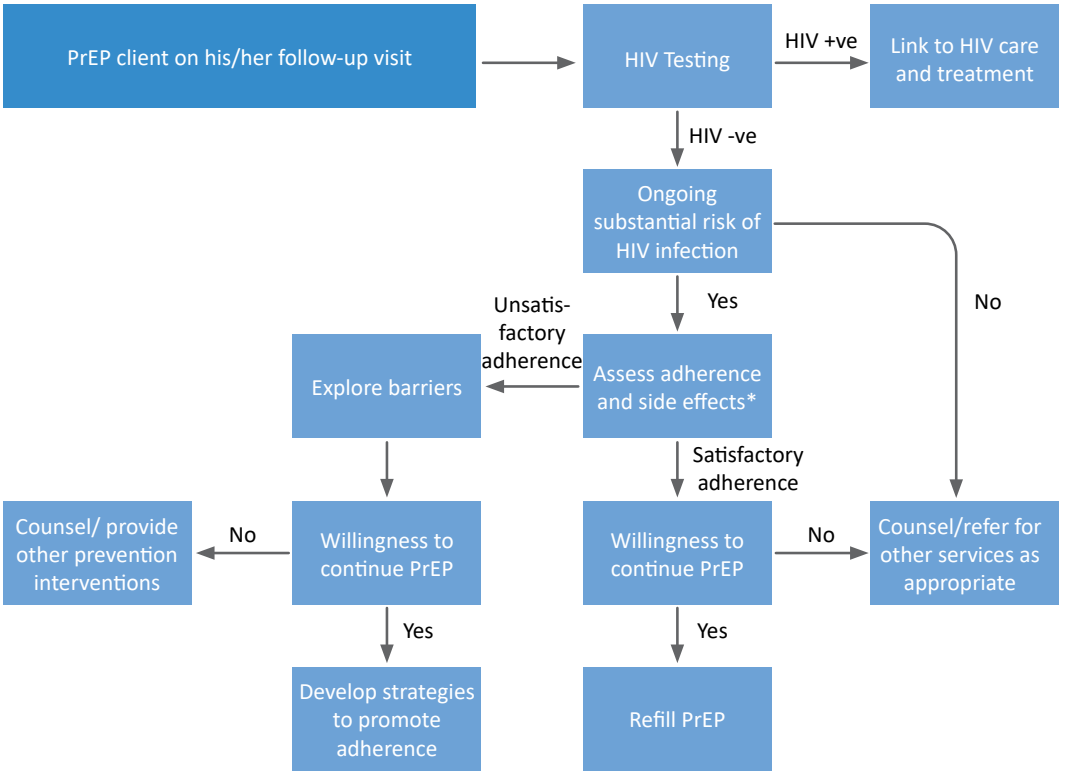
4 For those with signs and symptoms but no recent exposure to HIV in preceding 4 weeks, PrEP may be considered but additional HIV testing must be done at Month-2.

5 STOP PrEP if CrCl is less than 50 ml/min.

2. Follow-up visits

Repeat HIV Testing to confirm HIV negative status at one month after starting PrEP and every 3 months thereafter (M0, M1 and 3 monthly). Additional HIV testing at month 2 to be provided for those with the exposure within 4 weeks prior to PrEP (M0, M1, M2 and 3 monthly). Clinical assessment to assess signs and symptoms of acute HIV infection must be done every visit. Provide testing for other laboratory investigations as shown in "Table 1: Summary of Laboratory investigations for starting and monitoring PrEP". It is also necessary to assess the ongoing risk of the client regularly to determine whether to continue or discontinue PrEP. Address any adverse effects related to PrEP and refer/ manage accordingly. Continue providing counselling to explore any potential barriers to PrEP adherence and develop strategies to overcome if necessary. Provide/ Link with other combination prevention services as appropriate. The following flow chart illustrates the procedures to provide the PrEP clients on every follow up visit.

Flow Chart for PrEP Follow- Up



(*If there is any side effect, manage properly.)

Figure 4. Flowchart for PrEP follow-up

Table 3: Summary of Laboratory investigations for starting and monitoring PrEP

Name of the Test	Base line	Month 1	Month 3	Every 3 months	Other frequency (minimum)	Remark
HIV Test	✓	✓	✓	✓	n/a	For those with signs and symptoms of viral infection within 4 weeks prior initiation to PrEP, provide additional testing at month 2.
Creatinine	✓	n/a	n/a	n/a	Every 6 months	Check updated recommendations for creatinine monitoring in table 2
HBsAg	✓	n/a	n/a	n/a	n/a	If positive, please see “Hepatitis B infection” in Special Situations session for more information. If negative, consider vaccination against HBV.
AntiHCV	✓	n/a	n/a	n/a	Every 12 months	For populations at high risk of HCV infection
STI (Syphilis, GC, CT)	✓	n/a	n/a	n/a	Every 6 months	Syndromic or diagnostic STI testing, according to National STI Management Guidelines.
Pregnancy Test	n/a	n/a	n/a	n/a	n/a	When indicated.

IV. Monitoring and Management of PrEP Side Effects, Seroconversion and Other Special Situations

1. Management of Creatinine Elevation

Check estimated creatinine clearance (CrCl) every 6 months while taking PrEP for individuals 30 years and older and those younger than 30 years who have comorbidities.

- **If CrCl is > 50 ml/min:** Continue PrEP and recheck CrCl 6 monthly.
- **If CrCl decreases to less than 30 ml/min:** Discontinue PrEP.
- When **CrCl decreases to between 30 and 50 ml/ min:** Continue PrEP and test again after one month. If it remains between 30 and 50 ml/min, discontinue PrEP. Once PrEP is stopped, creatinine levels should be rechecked 3 months later and PrEP can be restarted if CrCl has returned to more than 50 ml/min. Clients with persistently reduced renal function (with CrCl less than 50ml/min after 3 months stopping PrEP) should be referred to physicians for clinical evaluation. Please see the following algorithm for management of Creatinine elevation.

Algorithm for management of creatinine elevation during PrEP follow-up visits

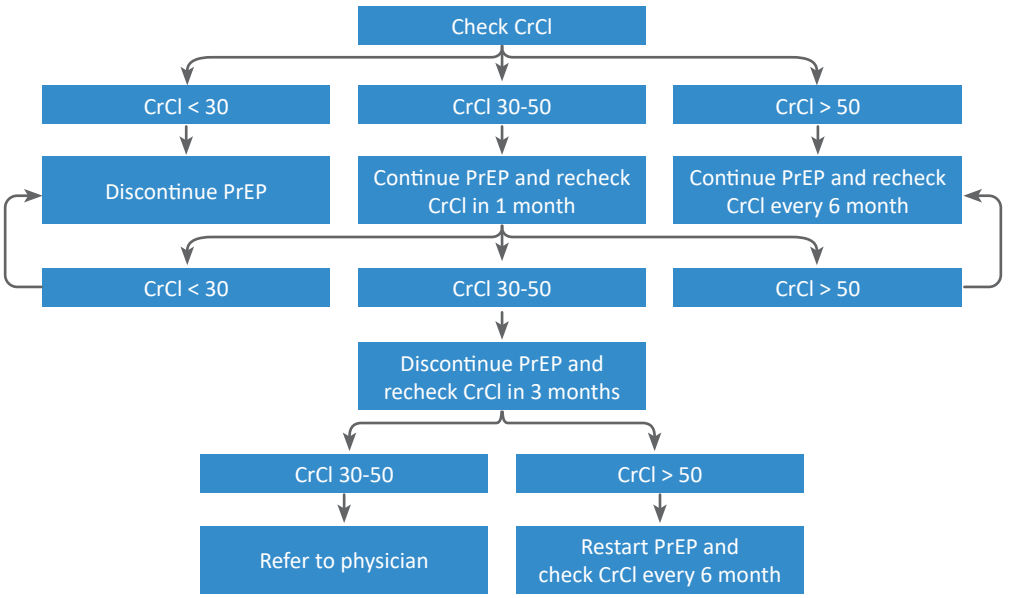


Figure 5. Algorithm for management of creatinine elevation

2. Management of Seroconversion

There is a risk of HIV seroconversion after receiving PrEP. While the majority of seroconversions happen in people with acute but undetected HIV infection at initiation, in people who have not taken PrEP as prescribed or in people who have stopped PrEP, PrEP failures can occur.

If a screening test of someone on PrEP is reactive at follow-up, stop PrEP and refer for confirmation test and follow National HIV Testing algorithm. ART can be offered as soon as possible after a confirmed positive HIV test result (seroconversion). The same NRTI's can be used in selecting ART regimen since the risk of drug resistance to them is low (<3%)[6]. If the confirmation test is negative and the client is still at substantial risk, restarting PrEP can be considered.

3. Discontinuation of PrEP

Clients may discontinue PrEP medication for several reasons, including personal choice, changed life situations resulting in lowered risk of HIV acquisition, intolerable toxicities, chronic[7] nonadherence to the prescribed dosing regimen despite efforts to improve daily pill-taking, or acquisition of HIV infection. Upon discontinuation for any reason, the following should be documented in the health record:

- HIV status at the time of discontinuation
- Reason for PrEP discontinuation
- Recent medication adherence and reported sexual risk behaviour

Any person who wishes to restart taking PrEP following discontinuation must undergo the same initiation evaluation as a person being newly prescribed PrEP, including an HIV test.

4. Hepatitis B Infection

All persons screened for PrEP should be tested for hepatitis B surface antigen (HBsAg) once, at or within one to three months of PrEP initiation. Lack of HBV testing should not be a barrier to PrEP initiation or use. Consider vaccination if HBsAg is not detected and there is no documented history of a completed vaccine series for Hepatitis B Virus (HBV). Clients with chronic HBV taking oral PrEP should be linked with HBV treatment as necessary. All persons screened for PrEP who test positive for HBsAg should be counselled prior to PrEP initiation that HBV will be well-controlled as long as they are taking daily oral PrEP. There is a small risk when PrEP is stopped that he/she may fall ill from hepatitis (unchecked HBV replication). Therefore, when PrEP is no longer needed or when

6 WHO implementation tool for PrEP of HIV Infection, Module 1 Clinical, Geneva: WHO, 2017

7 Repeated missed doses in six-month period and clients do not show willingness to continue PrEP

free supply of PrEP is no more available, regular monitoring to detect relapse and management of HBV after stopping TDF-based PrEP is important. TDF has a high genetic barrier to drug resistance, and HBV drug resistance against TDF is considered very rare.[8]

5. Hepatitis C Infection

Lack of HCV testing should not be a barrier to PrEP initiation or use. HCV antibody testing is strongly encouraged at or within one to three months of PrEP initiation and every 12 months thereafter where PrEP services are provided to populations at high risk of HCV infection. Individuals at substantial risk of HIV infection may also be at a higher risk for hepatitis C virus (HCV) infection. PrEP services provide an important opportunity to screen for HCV infection and provide linkages to care.

Hepatitis C infection is not a contraindication for TDF-based daily or event-driven oral PrEP use, and PrEP can be initiated before hepatitis C test results are available.

8 Differentiated and simplified pre-exposure prophylaxis for HIV prevention: Update to WHO implementation guidance. Technical Brief, Geneva: WHO, 2022

V. Minimizing PrEP Stigma and Role of the Community

Confidentiality is essential in PrEP services. People may face stigma if their PrEP use becomes known. PrEP use can exacerbate stigma if others mistakenly consider PrEP use to be evidence of irresponsible behaviour or if they mistakenly think that PrEP is HIV treatment. Such stigma will decrease PrEP uptake, continuation, and adherence among people who would otherwise benefit from it. PrEP, as an additional prevention service, should be integrated into existing service delivery points where other prevention services are available. Community awareness about PrEP should also be promoted. Presenting PrEP to communities as a responsible addition to the range of HIV prevention options available in Myanmar, that can protect both the PrEP user and his or her sexual and/or drug using partner(s), will increase the impact of PrEP and prevent more HIV infections.

It is very important to engage with the community for successful implementation of PrEP. Community members can play an important role in demand creation of PrEP in accordance with National Strategies as well as promotion of wider community engagement using both online and offline strategies. They can also contribute by participating in awareness raising, community-based screening of HIV and appropriate referral, and also providing counselling for PrEP in collaboration with Community Based Organizations and facilities where HIV services are provided.

VI. Counselling for PrEP

PrEP counselling before initiation as well as while taking PrEP is critically important for PrEP implementation to be successful as an additional prevention tool. PrEP counselling should include how PrEP works, importance of adherence and adherence strategies, follow-up visits, safety of PrEP and side-effects. The client should have very clear understanding of the protection provided by PrEP is not complete and does not prevent other STIs or unwanted pregnancies, and that therefore PrEP should be used as part of a package of HIV prevention services that includes condoms, lubricants, contraception, risk reduction counselling, harm reduction services and STI management. Clients should also be informed about how to stop and restart PrEP properly depending on their substantial risks, gender and use of hormones. Please see the following key messages for PrEP counselling.

1. Key counselling regarding PrEP efficacy

- **Effectiveness**

Message: PrEP is highly effective if you take it as prescribed.

[In clinical trials overall, the reduction in risk of acquiring HIV was more than 90% when PrEP was used consistently. Several large demonstration projects have observed no new HIV infections during PrEP use.]

- **Ways to support adherence**

Message: Taking PrEP each day is easiest if you make taking the tablets a daily habit, linked to something else that you do every day without fail.

[There are many ways to support adherence. For example, considering daily habits that could be linked with taking PrEP tablets, such as brushing teeth, after the evening meal, watching a daily television programme. Other ways to facilitate adherence include disclosing PrEP use to a partner or trusted person; using reminder devices, such as mobile phone alarms, can also be considered.]

Message: If you forget to take a tablet, take it as soon as you remember.

[Occasional use of two tablets of TDF/3TC or TDF/FTC a day is safe. Do not take more than two tablets per day.]

Message: PrEP tablets can be taken any time of day, with food or without food.

[PrEP can be taken with alcohol, although excess alcohol can be harmful to health and make people forget to take the PrEP tablets.]

Message: Taking PrEP is a responsible choice

[PrEP is a responsible way to protect oneself, one's sex partners and one's community. It is important to help the PrEP client cope with the fact that not everyone will understand their decision to use PrEP. Seeking support from their friends and other people who use PrEP can be helpful.]

Message: PrEP is safe and effective even if you are taking hormonal contraceptives, sex hormones or non-prescription medications

[There are no drug interactions between the PrEP medicines and hormonal contraception or sex hormones so they can be safely taken together. However, if anyone taking PrEP as population A wants to take sex hormones, there is a need to consult with doctor.]

- **Starting PrEP**

Message: Additional HIV prevention measures should be taken for 7 days after starting PrEP.

[PrEP provides high levels of protection in people who take PrEP medicines regularly. Time is needed to build up protective levels of the drug in the blood and other tissues. Additional HIV prevention should be taken for seven days. Ways to lower risk during this period include: adopting safer sexual practices, such as not having vaginal or anal intercourse, or using condoms for all vaginal and anal intercourse.

Remark: For population A, taking double dose (loading dose) 2-24 hours before possible sexual exposure, ideally closer to 24 hours, is sufficient.]

- **Stopping PrEP**

Message: You can stop PrEP 7 days after your last possible HIV exposure.

[PrEP can be stopped 7 days after the last possible exposure to HIV. People can consider stopping PrEP if they are no longer at substantial risk of acquiring HIV infection. Ways to lower risk include: adopting safer sexual practices, such as not having vaginal or anal intercourse, or using condoms for all vaginal and anal intercourse; changing circumstances such as leaving sex work or stopping injecting drug use; or, moving to a place that has a low prevalence of HIV infection such as states or regions with lower HIV prevalence than national HIV prevalence among adults over 15. For people in a serodiscordant relationship, HIV transmission risk is very low when the HIV-positive partner is virally suppressed on ART.

Remark: For population A, it is noted that stopping PrEP 2 days after last sexual exposure is sufficient.]

- **No PrEP interactions with recreational drugs or alcohol or Methadone Maintenance Therapy (MMT)**

Message: Taking alcohol or using recreational drugs such as heroin and other opioids, cocaine or methamphetamine or MMT will not reduce the effectiveness of PrEP and PrEP will not alter MMT dose.

[PrEP drug concentrations were comparable among users of cocaine and methamphetamine and people who denied the use of stimulants in a PrEP demonstration project. And it has no interaction with MMT. However, it should be noted that the use of those drugs would affect the adherence to taking PrEP.]

- **No STI protection (other than HIV infection)**

Message: PrEP does not prevent most sexually transmitted infections other than HIV. Condoms used in every act of sexual intercourse provide some protection against many of these infections.

[PrEP does not prevent syphilis, gonorrhoea, chlamydia, trichomonas or chancroid. PrEP provides some protection against acquisition of herpes in heterosexual populations and has decreased the incidence of genital ulcers in men who have sex with men and herpes infections in transgender women. Consistent use of condoms provides protection against many STIs, especially gonorrhoea and chlamydia, which are transmitted through the exchange of fluids rather than by skin-to-skin contact.]

- **No contraceptive effect**

Message: PrEP does not prevent pregnancy.

[The client should be encouraged to use effective contraception unless pregnancy is desired. PrEP medicines can be taken safely with all contraception methods. If a client wants to become pregnant, ways to become pregnant safely should be considered. PrEP can be used in pregnancy and during breastfeeding if HIV risk continues to be substantial during this time.]

Message: Oral, injectable or implant hormonal contraceptives do not significantly change the effectiveness of PrEP medicines, and PrEP medicines do not make hormonal contraceptives less effective.

[If anyone taking PrEP as population A wants to take sex hormones, there is a need to consult with doctor.]

2. Key counselling regarding PrEP safety

- **Testing**

Message: Get an HIV test before starting PrEP or restarting PrEP after you have stopped.

[PrEP is not sufficient for the treatment of HIV infection. HIV testing before starting or restarting PrEP is essential to detect infections that require treatment. HIV testing must follow National HIV Testing Algorithm. Use of PrEP in people who already have HIV infection can lead to development of resistance to PrEP medicines.]

- **Overall safety**

Message: PrEP is very safe.

- **Minor side-effects**

Message: About 10% of people who start PrEP will have some short-term, mild side-effects.

[Side-effects may include gastrointestinal symptoms (diarrhoea, nausea, decreased appetite, abdominal cramping or flatulence). Dizziness or headaches have also been experienced. Such side-effects are usually mild and resolve without stopping PrEP. Typically, these symptoms start in the first few days or weeks of PrEP use and last a few days, and almost always less than one month.]

- **Kidney side-effects**

Message: A very small percentage of people will not be able to take PrEP because they have problems with their kidneys.

[Blood testing for kidney function can be performed when clients start PrEP and while they are taking PrEP. Usually, a creatinine test is used. One-time elevations in serum creatinine are seen in approximately one in every 200 PrEP users, but usually levels return to normal on a second test.]

- **Hepatitis B and hepatitis C**

Message: You can have a blood test to see if you have hepatitis B and/or C infection.

[If a screening test for hepatitis B is negative, the client could benefit from a hepatitis B vaccination; if the test result is positive, the client can still take PrEP. HBV will be well- controlled as long as they are taking daily oral PrEP. There is a small risk when PrEP is stopped that he/ she may fall ill from hepatitis (unchecked HBV replication). Therefore, when PrEP is no longer needed or when free supply of PrEP is no more available, regular monitoring to detect relapse and management of HBV after stopping TDF-based PrEP is important. TDF has a high genetic barrier to drug resistance, and HBV drug resistance against TDF is considered very rare.

Consideration could be given to testing for evidence of Hepatitis C Virus (HCV) infection at or within 1-3 months of PrEP initiation and every 12 months thereafter where PrEP services are provided to populations at high risk of HCV infection. Testing for evidence of HCV infection is typically conducted by using a serological assay to detect antibodies to HCV (anti-HCV).]

- **PrEP during pregnancy and breastfeeding**

Message: You can use PrEP throughout pregnancy and breastfeeding.

[HIV infection can occur at high rates during pregnancy and breastfeeding. The risk of passing HIV infection onto a baby is higher if the mother becomes infected while she is pregnant. The existing safety data support the use of PrEP in pregnant and breastfeeding women who are at continuing substantial risk of HIV infection.]

VII. Annexes

Annex 1: Delivering PrEP in Myanmar

Annex 2: Tool for screening of Substantial Risk and Eligibility for PrEP

Annex 3: National HIV Testing Algorithm for HIV confirmation

Annex 4: Post-Exposure Prophylaxis (PEP)

Annex 1: Delivering PrEP in Myanmar

PrEP will be delivered in Myanmar either through Free Model or Co-pay/ Subsidized Model. In the Free Model, the clients will receive PrEP for free of charge. Cost related to taking PrEP including cost of PrEP medication, medical consultation, essential laboratory investigations will be fully covered. The PrEP demonstration project for MSM and TG populations has been conducted in Yangon, and one demonstration project for PWID population is planned in selected townships of Kachin State.

In addition, the NAP has been planning to expand PrEP program to other vulnerable populations and/or other states and regions to enable access to PrEP. Payment models will also be considered to cover the individuals who are willing to take PrEP but for whom the free-of-charge PrEP program is not feasible. In this model, facility-based HIV testing might be provided as a free service while remaining costs such as fee for the PrEP medication, consultation, cost for the investigations such as serum creatinine (2 times per year) and HBsAg screening at entry may be at the own expense of the client.

Differentiated PrEP service delivery

A differentiated PrEP service delivery approach is person- and community-centred and adapts services to the needs and preferences of people who are interested in and could benefit from PrEP. Differentiated PrEP services may make PrEP services more acceptable, accessible and support PrEP uptake, persistence and effective use.

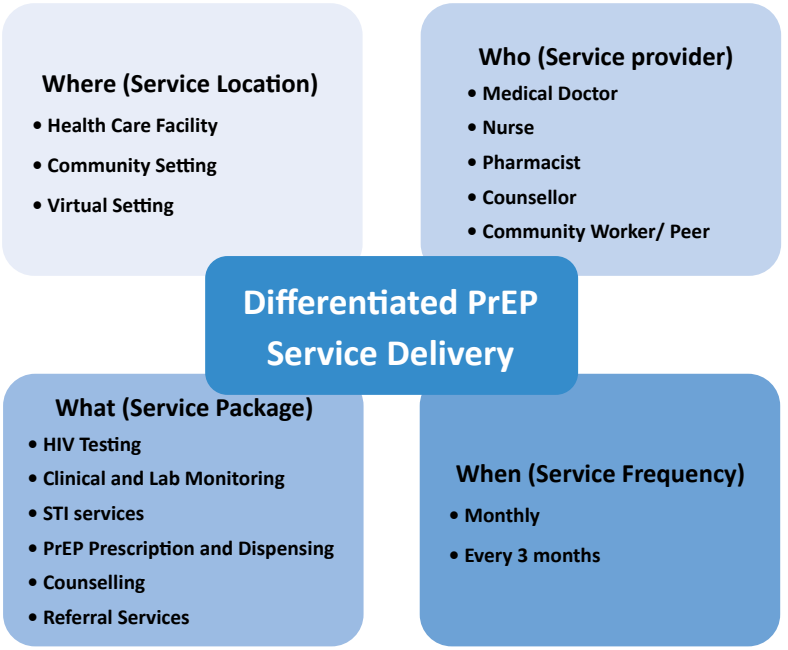


Figure 6. Building blocks of differentiated PrEP service delivery

The following differentiated PrEP service delivery approaches (including community-based, pharmacies and online) should be considered based on programmatic needs and feasibility as part of broader effort to increase reach of PrEP services to targeted communities.

- PrEP promotion and provision in community-led key population service center (KPSC) and prevention service facilities
- PrEP distribution models (established points, pharmacies, telehealth, PrEP express [combined online registration and fast-track facility visit])

It is still critical to ensure linkages to other services as necessary while providing differentiated PrEP service delivery.

Public Private Partnerships

The services provided for PrEP in the private sector will be complementary to the public sector and will contribute towards expanding access to quality PrEP services. A structured engagement process of the private sector should be implemented.

Private providers such as the Specialist Hospitals/Clinics/General Practitioners who are interested in provision of PrEP will be networked and coordinated by an organization body, for example, Myanmar Medical Association (MMA) or other dedicated NGOs.

Minimum standards should be developed and set for selecting providers by these organizations in close collaboration with NAP.

These organizations are also responsible for quality provision of PrEP services by their providers and should ensure providers are following the national guidelines, complying the use of nationally standardized records and registers, and sharing the report.

NAP will lead the price negotiation of PrEP medicine with pharmaceutical companies in the market for the private providers under this network. NAP will also provide required capacity building activities and conduct monitoring and supervision activities to ensure the quality of services.

Annex 2: Tool for screening of Substantial Risk and Eligibility for PrEP

Pre-Exposure Prophylaxis (PrEP) Screening for Substantial Risk and Eligibility

1. Facility Information	
Facility Name	
Date of Initial Client Visit *(dd/mm/yyyy)* __ __ /__ __ /__ __ __ __	Person Completing Form

2. Client Information	
Name	PrEP ID Number: ☐☐\☐☐☐ \☐☐☐☐☐ \☐☐ **Program code - alphabets (2#)\clinic code No. (3#)\patient No. (5#)\ yr No. (2#)**
Address Village/City, Township, State or Region – Dropdown MIMU list	Telephone #
Father or Mother's Name:	Township of birth: (dropdown MIMU list)
NRC Number:	Master Patient Index Number (12 digits):

3. Client Demographics				
What was your sex at birth?	☐ Male	☐ Female	☐ Other *(specify)*: _____	
What is your age? *(Specify number of years.)* _____ *Date of birth (if feasible) (dd/mm/yyyy):* __ __ /__ __ /__ __ __ __				

4. Sexual and Drug Injection Core Risk Classification				
1. Do you consider yourself: male, female, transgender, or other? ❑ Male ❑ Female ❑ Transgender woman, ❑ Other *(specify)*: _____				
2. Do you have sex with:	❑ Men / TG W response	❑ Women only	❑ Both men and women	❑ No
3. Have you exchanged sex as your main source of income in the last 6 months?	❑ Yes	❑ No	❑ No response	
4. In the last 6 months, have you injected illicit or illegal drugs?	❑ Yes	❑ No	❑ No response	

5. Key Population Classification (an individual can belong to more than one category)	
If client answers "Male" to question 1 and answers "Men / TG W" or "Both men and women" to question 2, then categorize as man who has sex with men (MSM)	❑
If client answers "Transgender TG W" to question 1, then categorize as transgender (TG W)	❑
If client answers "Yes" to question 3, then categorize as sex worker (SW)	❑
If client answers "Yes" to question 4, then categorize as person who injects drugs (PWID)	❑
If client is not transgender woman (TG W) and answers "No" or "No response" to questions 2 to 4, classify as None Key Population	❑

	Final Classification: *(Mark ALL that apply*)*	**Some clients may belong to more than one category due to overlapping risk behavior.*
Man who has sex with men (MSM)	❑ MSM	
Transgender (TG W)	❑ TG W	
Sex worker (SW)	❑ SW	
Person who injects drugs (PWID)	❑ PWID	
Other *(specify)*	❑ Other(*specify*):_____	
None	❑ None Key Population	

6. Screening for Substantial Risk for HIV Infection	
Client is at substantial risk if he/she belongs to categories ❶, ❷, ❸ or ❹ *below*	**Question Prompts for Providers**
❶ **If client is sexually active in a high HIV prevalence population PLUS reports ANY one of the below in the last 6 months**	Have you been sexually active in the last 6 months?
☐ Reports vaginal or anal intercourse without condoms with more than one partner	In the last 6 months, did you have sex with vaginal or anal intercourse more than one partner? In the last 6 months, did you use condoms consistently during sex?
☐ Has a sex partner with one or more HIV risk:	In the last 6 months, have you had a sex partner who: • Is living with HIV? • Injects drugs? • Has sex with men? • Is a transgender person? • Is a sex worker? • Has sex with multiple partners without condoms?
☐ History of a sexually transmitted infection (STI) *based on self-report, lab test, syndromic STI treatment*	In the last 6 months, have you had an STI by lab testing or self-report or syndromic STI treatment?
☐ History of use of post-exposure prophylaxis (PEP)	In the last 6 months, have you taken post-exposure prophylaxis (PEP) following a potential exposure to HIV?
☐ Requesting PrEP	If the client request PrEP by him / herself.
❷ **If client reports history of sharing injection material or equipment in the last 6 months** ☐ History of sharing injection material or equipment	In the last 6 months, have you shared injecting material with other people?
❸ **If client reports having a sexual partner in the last 6 months who is HIV positive AND who has not been on effective* HIV treatment** ☐ History of HIV-positive sex partner not on effective treatment *Other than * question, consider the client has the history of HIV positive sex partner not on effective treatment if the client responds no.*	Is your partner HIV positive? If yes, is he/she on ART? If yes, is he/she on ART for more than 6 months? If yes, is he / she suspected poor adherence to ART? If yes, is he / she detectable viral load result? Is your couple trying to conceive*?
❹ ☐ Requesting PrEP	If the client request PrEP by him/ herself

7. Acute HIV Infection			
Ask the client: In the past 72 hours, have you had sex without a condom with someone whose HIV status is positive or not known to you, or have you shared injection equipment with someone whose HIV status is positive or unknown to you?	☐ **Yes***	☐ No	☐ Don't know
In the past 28 days, have you had symptoms of a cold or flu, including fever, fatigue, sore throat, headache, or muscle pain or soreness?	☐ **Yes****	☐ No	☐ Don't know

*** If the client reports potential exposure to HIV within past 72 hours, do NOT offer PrEP. Follow facility procedures to evaluate further or refer for evaluation for post-exposure prophylaxis (PEP).**

**** If the client reports flu-like symptoms or other signs of acute HIV infection, AND recent exposure to HIV infection, do NOT offer PrEP and evaluate further, following facility procedures to diagnosis acute HIV infection.**

8. PrEP Eligibility	
Client is eligible if he/she fulfills ALL the criteria below:	
☐ **HIV non reactive / negative**	**Date client tested:** *(dd/mm/yyyy):* __ __ /__ __ /__ __ __ __ **Date client received screening test results:** *(dd/mm/yyyy):* __ __ /__ __ /__ __ __ __ **Screening test result** ☐ Non-reactive ☐ Reactive **If screening test, reactive** **Date client received confirmation test results:** *(dd/mm/yyyy):* __ __ /__ __ /__ __ __ __ **Confirmation Test result:** ☐ Negative ☐ Positive *(Refer to HIV medical care.)* ☐ Inconclusive *(Re-test in 14 days.)*
☐ **At substantial risk of HIV**	At least one item/risk in Section #6 above is ticked
Has no suspicion of acute HIV infection? ☐ Yes ☐ No ☐ Unknown	See Section #7 below to confirm no suspicion of AHI
If all boxes in Section 8 are ticked, offer PrEP.	

9. Services Received by Client

☐ **PrEP offered.**

- ☐ **PrEP accepted.**
- ☐ **PrEP declined.** (*If declined, see* Reasons for Declining PrEP, *below).*

Date eligible *(dd/mm/yyyy):* __ __ /__ __ /__ __ __ __

Date initiated *(dd/mm/yyyy):* __ __ /__ __ /__ __ __ __ *Same-day initiation recommended.*

Reasons for Declining PrEP

(Check all that apply.)

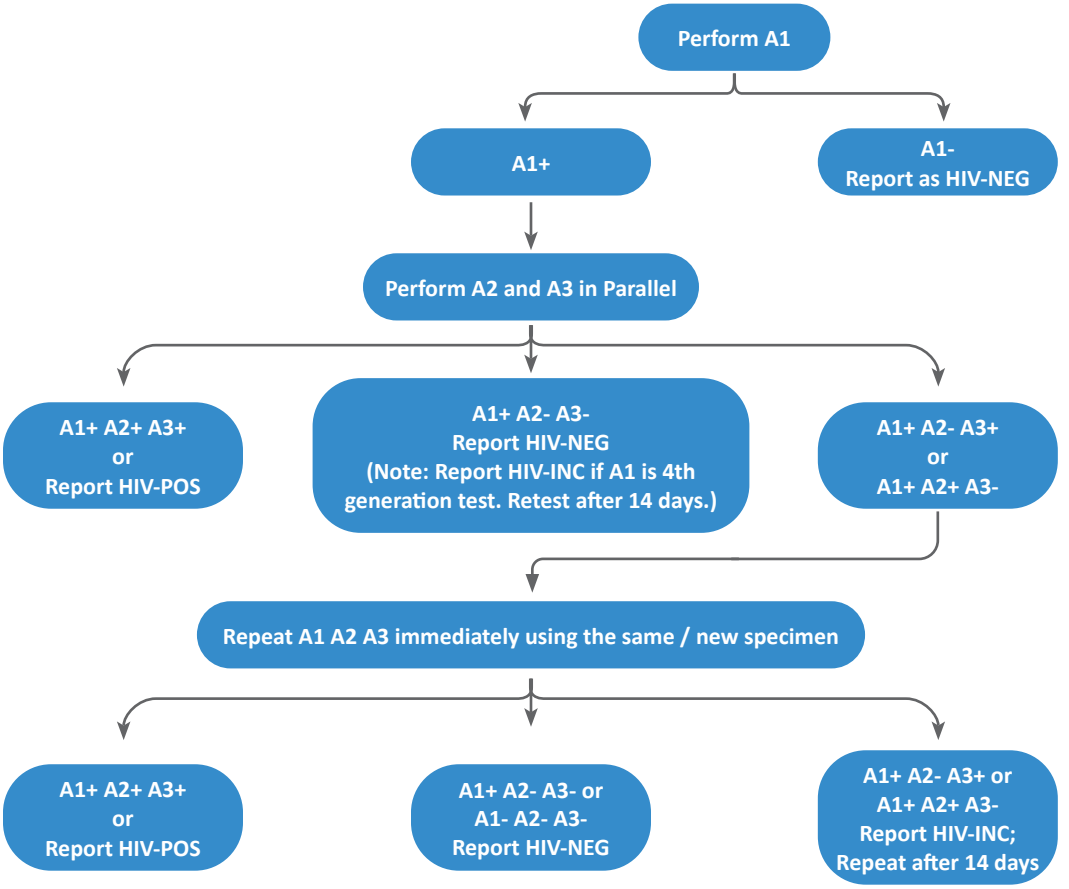
☐ **Does not think it necessary**
☐ **Does not wish to take a daily medication**
☐ **Concerns about side effects**
☐ **Concerns about what others might think**
☐ **Concerns about time required for clinic follow-up**
☐ **Concerns about safety of medication**
☐ **Concerns about effectiveness of medication**
☐ **Other** *(specify):*

☐ **Referred for PEP evaluation**

☐ Referred for HIV confirmation (if HIV screening test reactive)

☐ **Referred for PCR/HIV Ag test or follow-up HIV re-testing (if suspicion of acute HIV infection or HIV test inconclusive)**

Annex 3: National HIV Testing Algorithm for HIV confirmation



Recommended rapid test kits for 3-assay HIV Testing Strategy are:

A1 = Alere Determine HIV-1/2 (manufactured by Alere Medical Co., Ltd., Japan) (D) ICT (sensitivity 100% and specificity 99.75%)

If not available, WHO pre-qualified RDT with 100% sensitivity and specificity similar to Determine.

A2 = Uni-Gold HIV (manufactured by Trinity Biotech Manufacturing Ltd., Ireland) (UG) ICT (sensitivity 100% and specificity 100%)

A3 = HIV 1/2 STAT-PAK (manufactured by Chembio Diagnostic Systems Ltd., USA) (SP) ICT (sensitivity 99% and specificity 100%)

Annex 4: Post-Exposure Prophylaxis (PEP)

People who have been exposed to HIV in the preceding 72 hours should be offered PEP. PEP should be offered as soon as possible after exposure. A full 28-days prescription of antiretroviral drugs should be provided for PEP following initial risk assessment. Enhanced adherence counselling is suggested for all individuals initiating PEP. After 28 days of PEP, PrEP can be started without a gap if the HIV test remains negative and there is substantial ongoing risk of HIV acquisition.

A regimen for PEP for HIV with two ARV drugs is effective, but three drugs are preferred.

- TDF + 3TC (or FTC) is the preferred backbone.
- The third drug can be anyone of the following: LPV/r, ATV/r, EFV or DTG.

References

1. World Health Organization. Differentiated and simplified pre-exposure prophylaxis for HIV prevention: update to WHO implementation guidance; Technical Brief, 2022.
2. National AIDS Programme. Guidelines for the clinical management of HIV infection in Myanmar. Fifth edition. Department of Health, Ministry of Health and Sports, Myanmar, 2017
3. National AIDS Programme. Myanmar guidelines on HIV testing services. Ministry of Health and Sports, Myanmar, 2019.
4. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Recommendation for a Public Health Approach, Geneva: World Health Organization, 2016
5. WHO implementation tool for PrEP of HIV Infection, Module 1 Clinical, Geneva: WHO, 2017
6. Prequalified in vitro diagnostics products, WHO at https://extranet.who.int/pqweb/vitro-diagnostics/vitro-diagnostics-lists accessed in Dec 2022
7. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Recommendation for a Public Health Approach, 2nd edition. Geneva: World Health Organization, 2016.
8. The U.S. Centers for Disease Control and Prevention. Pre-Exposure Prophylaxis for The Prevention of HIV Infection in the United States, 2017.
9. ICAP at Columbia University. Pre-Exposure Prophylaxis (PrEP) Training for Providers in Clinical Settings, 2019.
10. PrEP Service Delivery SoPs/tools developed by LVCT Health for IPCP PrEP demonstration project, 2016.
11. ASHM. Decision Making in PrEP, 2018.