
# IMPLEMENTATION MANUAL FOR PRE – EXPOSURE PROPHYLAXIS (PrEP) OF HIV INFECTION

**THE FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA,**

**MINISTRY OF HEALTH**

**December 2019**

**Addis Ababa, Ethiopia**

## LIST OF ACRONYMS

| | |
|---|---|
| **AIDS** | **Acquired Immune Deficiency Syndrome** |
| **ART** | **Anti-Retroviral Treatment** |
| **CDC** | **Center for Disease Control** |
| **DIC** | **Drop-in-Center** |
| **EDHS** | **Ethiopian Demographic Health Survey** |
| **EPHI** | **Ethiopian Public Health Institute** |
| **EPSA** | **Ethiopian Pharmaceutical Supply Agency** |
| **FHAPCO** | **Federal HIV Prevention and Control Office** |
| **FMoH** | **Federal Ministry of Health** |
| **FSW** | **Female Sex Worker** |
| **HIV** | **Human Immune deficiency Virus** |
| **ICAP** | **International Center for AIDS Care and Treatment Program** |
| **MARPs** | **Most at Risk Populations** |
| **MoH** | **Ministry of Health** |
| **PITC** | **Provider Initiated HIV Testing and Counseling** |
| **PSI** | **Population Services International** |
| **PrEP** | **Pre – Exposure Prophylaxis** |
| **RHB** | **Regional Health Bureau** |
| **STIs** | **Sexually Transmitted Infections** |
| **USAID** | **United States Agency for International Development** |
| **VCT** | **Voluntary Counseling and Testing** |
| **WHO** | **World Health Organization** |

**FORWARD**

In Ethiopia, HIV epidemic is low intensity, mixed epidemic type with significant heterogeneity across geographic areas and population groups. The national HIV prevalence is estimated to be 0.9%, urban are more affected than rural areas (2.9% versus 0.4%) while females are twice as affected as male (1.2% versus 0.6%). During the last two decades, the country responded vigorously to curb the epidemic through multi-sectoral approach involving all stakeholders, mobilizing resources and the community at large.

The introduction of anti-retroviral drugs and all biomedical prevention methods helped significantly to reduce the mortality, morbidity as well as transmission of the virus. Pre Exposure Prophylaxis of HIV(PrEP) is one of the biomedical prevention methods that came in to practice very recently for public use that will have significant impact to further decrease the transmission of HIV among those population group with substantial risk.

Based on the experience from other countries and pilot project conducted at some public health facilities and DICs among high-risk population groups, female sex workers and negative partners of discordant couples, providing PrEP for these sub-population groups has a big demand and acceptance. Based on this, the Federal Democratic Republic of Ethiopia, involving development partners, planned to scale-up PrEP service among Female Sex workers and negative partners of discordant couples nationally and revised this implementation manual to be used for scale up of the service at health facilities and Drop in Centers that provide ART services.

State Minister of Health

**ACKNOWLEDGEMENT**

The MOH Acknowledges all partner organizations involved on this initiative while conducting the PrEP piloting and developing this scale-up implementation manual. The ministry also recognizes experts listed below for their contributions in development and revision PrEP implementation manual, training material, job aides and other related tools.

| **Name** | **Organization** |
|---|---|
| Mrs. Mirtie Getachew | FMoH |
| Dr. Zerihun Hika | FMoH/ICAP |
| Mrs. Genet Getachew | FMoH |
| Dr. Leul Endale | FMOH |
| Dr. Yoseph Gutema | ICAP |
| Samrawit Ejigu | PSI |
| Dr. Zelalem Tesfaye | ICAP |
| Dr. Cassia Wells | ICAP at Columbia university |
| Dr. Emily Gwavava | PSI- Zimbabwe |
| Asmamaw Sileshi | CHAI |
| Dr. Fahmi Ahmed | WHO |
| Israel Lema | PSI |
| Dr. Fethia Kedir | PSI |
| Dr. Teklu Weldegebriel | USAID |
| Gizachew Eyassu | USAID |
| Dr. Mesfin Girma | ICAP |
| Shakir Jemal | PSI |
| Dr. Nehgist Tesfaye | UNAIDS |

**CONTENTS**

## I. BACKGROUND

HIV continues to be a major global public health issue. In 2018, an estimated 37.9 million people were reported to be living with HIV with a global HIV prevalence of 0.8% among adults (UNAIDS 2019 report).

The current HIV epidemic in Ethiopia is low intensity, mixed epidemic type with significant heterogeneity across geographic areas and population groups. The national HIV prevalence is estimated to be 0.9%, urban are more affected than rural areas (2.9% versus 0.4%) while females are twice as affected as male (1.2% versus 0.6%). Out of the 11 regional states and city administrations, seven have HIV prevalence of 1% and above. Key and priority populations (KP & PP) are disproportionally affected compared with the national average: 23% among Female Sex Workers (FSW), 4.9% long-distance truck drivers (EPHI 2013). According to 2016 EDHS, the prevalence of HIV among married couples is 1.1 out of which 72% have discordance results. In Ethiopia, there are still …….new infections annually mostly affecting the KP & PP groups. From WHO's recommendation, Pre Exposure Prophylaxis (PrEP) of HIV is one of the interventions that help countries to reduce new HIV infection.

The Federal Ministry of Health (FMoH) and development partners, by involving all stakeholders and the community, are moving towards achieving epidemic control and have committed to meet the 2030 UNAIDS targets of 95-95-95, to end HIV transmission by 2030 and reduce HIV as a public health threat.

## II. RATIONALE

Global evidence show that PrEP is effective infection reduction intervention when properly combined with other HIV prevention services. Even though there are good progress in the country in reducing new infection, there is still a significant number of new HIV infections per year. To avert this ongoing new HIV infection, a combination HIV prevention approach including PrEP as an additional component is crucial. Combination HIV prevention is an approach that seeks to achieve maximum impact for preventing new HIV infections by combining biomedical, socio-behavioral, and structural interventions that are human-rights based and evidence-informed, in the context of a well-researched and understood local epidemic.

Considering this, PrEP is endorsed in the national comprehensive HIV Prevention, care and treatment guideline and HIV prevention roadmap (2018-2020). Following this MoH in collaboration with partners has piloted PrEP as an additional HIV prevention service in nine public health facilities and six Drop-in-Centers (DICs). The finding of the pilot implementation showed that the service is acceptable among the national target groups. Moreover, the service is feasible to be implemented nationally from the pilot experience and creates a good opportunity for HIV case identification, STI diagnosis and management as well as risk reduction counseling for those who have substantial risk of HIV infection. Therefore, it is worth to scale up PrEP service nationwide to contribute to the reduction of new HIV infection.

## III. BASIC CONCEPTS OF PREP

**Pre – Exposure Prophylaxis (PrEP):** Defined by the World Health Organization, as the use of antiretroviral drugs by HIV-negative people, before potential exposure to prevent the acquisition of HIV. Oral PrEP is an evidence-based HIV risk-reduction intervention that is offered to all people at substantial risk of acquiring HIV**.**

**Substantial risk of HIV infection:** Defined by the WHO, as a population group with an HIV incidence greater than 3 per 100 person–years in the absence of PrEP**.**

The nationally selected for PrEP drug is a fixed dose combination that contains Tenofovir 300mg and Lamivudine 300mg daily for the identified target groups with substantial risk for HIV infection.

## IV. TARGET BENEFICIARIES:

The target beneficiaries for PrEP service in Ethiopia are consenting HIV Negative FSWs and HIV negative partners of sero – discordant couples.

## V. OBJECTIVE

This implementation manual serves as a reference material for providing guidance to support national scale-up implementation of PrEP. This manual addresses the national target groups, basics of PrEP, eligibility criteria, PrEP monitoring and follow up.

## VI. TARGET AUDIENCES

The target audiences of this implementation manual are:

• Health care workers (physicians, health officers, nurses, pharmacy personnel, laboratory Personnel) and case managers/adherence supporters/mother support groups

•HIV program managers, health planners, and researchers

•Organizations involved in antiretroviral drug procurement, supply management, and ART Service delivery

•Community and faith-based organizations working on HIV programs including PLHIV

## VII. IMPLEMENTATION OF PREP

Based on the pilot findings from the implementation of PrEP in the country and lessons learnt, MoH has launched national scale up of the service to be offered in all ART providing facilities. Hence, the following activities/issues should be considered during implementation:

- Demand creation- Targeted awareness creation activities on PrEP service availability for the targeted group. This needs to be implemented by policy makers, program managers, service providers and community (Peer educators/Peer navigators). Mass media, Job aids, client education materials other provider support tools will be used to increase awareness creation.
- **For HIV negative partners of sero - discordant couples**, adherence case managers and service providers will identify partners with continuous risk of HIV infection such as newly identified sero-discordant couples and their virally unsuppressed partner. The selection of eligible beneficiaries will also be done through using the existing index case register and line-listing HIV negative partners of sero – discordant couples, who will be contacted and offered evaluation for PrEP eligibility.

- National level training will be provided to participants selected from regions who can cascade the skills to offer the service.
- Good quality counseling is key for successful PrEP service roll-out; clients should be offered ongoing counseling service by providers for optimal enrollment and maximized adherence required for success of the service. Service providers counseling skill needs to be built through ongoing mentoring and training.
- The health care providers, in collaboration with the adherence Case Managers, serving at both ART and PMTCT units of health facilities, will be involved in the selection of the HIV negative partners of sero – discordant couples and negative FSWs. The selection will be made through eliciting contacts of index clients, or after conducting reviews to the ICT register and line listing all HIV negative partners. Then the index client will be asked to bring the HIV negative partner to the facility, and counseling and education about PrEP will be provided to the index clients and partners.
- HIV negative FSW and HIV negative partners of sero - discordant couples, who consent and fulfill the eligibility criteria, will be enrolled in the PrEP service.
- Required supplies at service providing sites: HIV test kit, ART drugs(TDF/3TC)
- Services such as HBsAg, pregnancy test and renal function test at service delivery sites/through referrals
- Acute viral syndrome; consider re-testing in 1 month before PrEP initiation. Acute HIV infection is symptomatic 40 – 90 % of the time, including signs and symptoms of fever, sore throat, aches and pains, lymphadenopathy (swollen glands), mouth sores, headache or rash.
- Pregnancy and breastfeeding; PrEP can be offered and continued even if the beneficiaries are pregnant or breastfeeding.
- The risk of HIV drug resistance to either TDF or 3TC is low, occurring in approximately 1 in 1,000 PrEP users in clinical trials, and was mainly seen in those with acute undetected HIV infection at the time of initiating PrEP.
- Young adults, as well as FSWs may benefit from appointments that are more frequent e.g. monthly visits, as they commonly have lower adherence rates.
- Adherence is a significant modifier of PrEP effectiveness and PrEP can be started and stopped as a person moves through “seasons of risk”.

- Offer immediate ART if a PrEP user sero - converts.
- Minimize PrEP stigma by educating clients that taking PrEP is a responsible choice to protect themselves and their sexual partners from HIV infection.
- Referral linkages (transfer-in and transfer-out) and feedback tracking should be facilitated for clients who request a change of service sites.

## VIII. ELIGIBILITY CRITERIA

Health care providers will participate actively in the provision of education and counseling for potential beneficiaries or users about PrEP, which will be provided as part of a combination HIV prevention package. The following are the eligibility criteria used to identify participants PrEP service among the target population group.

**Table – 1: Eligibility criteria for PrEP**

| **HIV Negative FSWs** | **HIV Negative Partners of Sero – Discordant Couples** |
|---|---|
| • HIV negative using a rapid antibody test as per the National HIV testing algorithm on the day of PrEP initiation<br>• No suspicion of acute HIV infection<br>• Self- identifying FSWs.<br>• No contraindications to PrEP medicines (TDF/3TC) | • HIV negative using a rapid antibody test as per the National HIV testing algorithm on the day of PrEP initiation<br>• No suspicion of acute HIV infection<br>• Substantial risk of HIV infection (any ONE of the following in the past six months):<br>○ Has a known HIV positive sexual partner(s) who is not on ART or<br>○ On ART less than six months, or not yet achieved viral suppression or<br>• No contraindications to PrEP medicines (TDF/3TC) |

| | |
|---|---|

## IX. THE EXCLUSION CRITERIA AND CONTRAINDICATIONS FOR PrEP ( this all be done for those identified using the eligibility criteria before starting the Prep MEDICATION)

- Finding of HIV infection (existing HIV infection should be ruled out by testing using the national algorithm on the same day of PrEP initiation).
- Finding of Signs/symptoms of acute HIV infection, with probable recent exposure to HIV.
- Estimated creatinine clearance of less than 60 ml/min (if known).
- Client reported allergy or there is contraindication to any medicine in the PrEP regimen.
- Finding of Hepatitis B infection (clients with HBsAg Positive test result).
- Unwillingness or not being ready to use PrEP as prescribed and/or give detail information required for tracing.
- Age less than 18 ( unless there is special program that provide ART/PrEP service for sexually active minors who are less than 18 years age)

**Other important considerations include**:

- Testing for **Hepatitis – B** is mandatory before initiation and if a client is positive for **Hepatitis B infection**, referrals should be facilitated/made to health facilities offering management for Hepatitis B infection. Clients with such results will not be initiated on PrEP.

## X. FOLLOW – UP AND MONITORING OF PREP

**Prescription Intervals:**

**For HIV negative partners of sero - discordant couples:**

- At initiation: provide a 1-month supply
- At one – month: repeat HIV test and provide 3 months supply

- Every 3 – months: repeat HIV test and provide 3 months supply

**For HIV negative Female sex workers**

FSW benefit from monthly clinic visits to address their changing routines and multiple health needs. During each visit, every other component of combination HIV prevention package has to be offered to PrEP users.

- At initiation: provide a 1 – month supply
- At one – month: repeat HIV test, provide a 1 – month supply, and for the first 3 – months, appointments monthly for close adherence support and provision of other prevention packages.
- At three – months: repeat HIV test and provide 3 – months supply. If the client requests for monthly visits, provider should consider monthly supply.

**Initial follow –up visits**

**Table – 2: Initial visit procedures**

| **INVESTIGATION / INTERVENTION** | **RATIONALE** |
|---|---|
| HIV test (using the national algorithm for HIV testing services as per the guidelines) | To assess HIV infection status.<br>To complete a symptom checklist for possible acute HIV infection. |
| Serum creatinine( if available) | To identify pre-existing renal disease (estimated creatinine clearance less than 60 ml/min). Calculate creatinine clearance using age, sex and weight. |
| Hepatitis B surface antigen | If negative, provide PrEP.<br>If positive, refer for further testing and assessment for hepatitis B treatment. |
| Screening for sexually | To diagnose and treat STI (syndromic or diagnostic STI testing, depending on local guidelines). |

| | |
|---|---|
| transmitted infection (STI) | |
| Pregnancy testing | To guide antenatal care, contraceptive and safer conception counselling, and to assess risk of mother to child transmission. Pregnancy is not a contraindication for PrEP use (see section below). |
| Counseling | To assess whether the client is at substantial risk of HIV.<br>To discuss prevention needs and provide condoms<br>To develop a plan for effective PrEP use and successful adherence<br>To assess fertility intentions and offer contraception or safer conception counselling.<br>To assess intimate partner violence and gender-based violence.<br>To assess substance use and mental health issues. |

**Table – 3: Follow – up after initiation**

| **Confirmation of HIV-negative status** | **Every 3 months. Consider also testing at 1 month.** |
|---|---|
| Address side-effects | Every visit. |
| Brief adherence counselling | Every visit. |
| Estimated creatinine clearance | Every 6 months. Consider more frequently if there is a history of conditions affecting the kidney, such as diabetes or hypertension; |
| Screening for sexually transmitted infection (STI) | To diagnose and treat STI (syndromic or diagnostic STI testing, depending on local guidelines). Every visit. |
| Counseling | To assess adherence and provide counselling regarding effective PrEP use<br>To assess whether the client is still at substantial risk of HIV.<br>To discuss prevention needs and provide condoms<br>To assess fertility intentions and offer contraception or safer conception counselling.<br>To assess intimate partner violence and gender based violence. |

| | |
|---|---|
| | To assess substance use and mental health issues. |

HIV testing must be performed before PrEP is initiated. Additional HIV testing that is conducted one month after PrEP initiation, is used to help detect acute HIV infection that may have been incubating when PrEP was initiated. HIV testing should also be conducted when PrEP is restarted. Testing for HIV should be conducted every three months while clients are on PrEP.
It should be made clear that PrEP should not have to be considered as treatment for HIV, despite using the same medications, and therefore it should not be shared with people who have not tested HIV negative.

## XI. SIDE EFFECTS OF PrEP DRUGS

TDF/3TC are generally well tolerated; Common side effects are usually mild and self-limiting (Approximately 1 in 10 individuals in the first 1 - 2 months), and do not require discontinuation of PrEP. Major side effects are rare.

- 1 in 10 PrEP users may have side – effects such as nausea, abdominal cramps, headache; these are usually mild and resolve over the first month of taking PrEP.
- 1 in 200 may have creatinine elevation (typically reversible, if PrEP is stopped).
- 1 % average loss of bone mineral density; this also recovers after stopping PrEP.

**POTENTIAL SIDE EFFECTS**

**Major side effects:** These include renal toxicity and metabolic complications (decreased bone mineral density, which is reversible in adults upon stopping PrEP), extremely small risk of lactic acidosis and hepatic steatosis or steato– hepatitis.

**Minor side effects:** These include gastrointestinal symptoms (diarrhoea, nausea, vomiting and flatulence), which are self-limiting and typically end within first month of use; unintentional weight loss.

**Less predictable side effects:** These could be hypersensitivity reactions and flares of hepatitis B in those who are chronic carriers if they stop TDF / 3TC.

**Clients who test HIV positive prior to initiation of PrEP**

Clients who test HIV positive must also be linked to HIV care and treatment, and support and offer ART as soon as possible (as per the national guideline), their partners should be encouraged to test for HIV.

**Clients who test HIV positive after initiation of PrEP**

HIV seroconversion after initiating PrEP can occur and may be due to non – adherence or being during the window period at the time of testing. As soon as an HIV positive test result is confirmed, the client must be linked to HIV care and treatment and initiate on ART using first - line regimens.

**Adherence and Retention of PrEP Users**

After clients have initiated PrEP, the core focus of the service provider/ case managers should be on supporting retention and maintaining adherence among those using PrEP. At each follow – up visit, health care providers should assess for any changes in adherence. Health care providers should provide support to clients to identify strategies for improving adherence, which take into consideration a clients' individual barriers and facilitators of adherence. There should be ongoing client-centered adherence counseling and education to encourage combination HIV prevention practices during each PrEP follow-up visits.

## XII. DISCONTINUATION OF PrEP

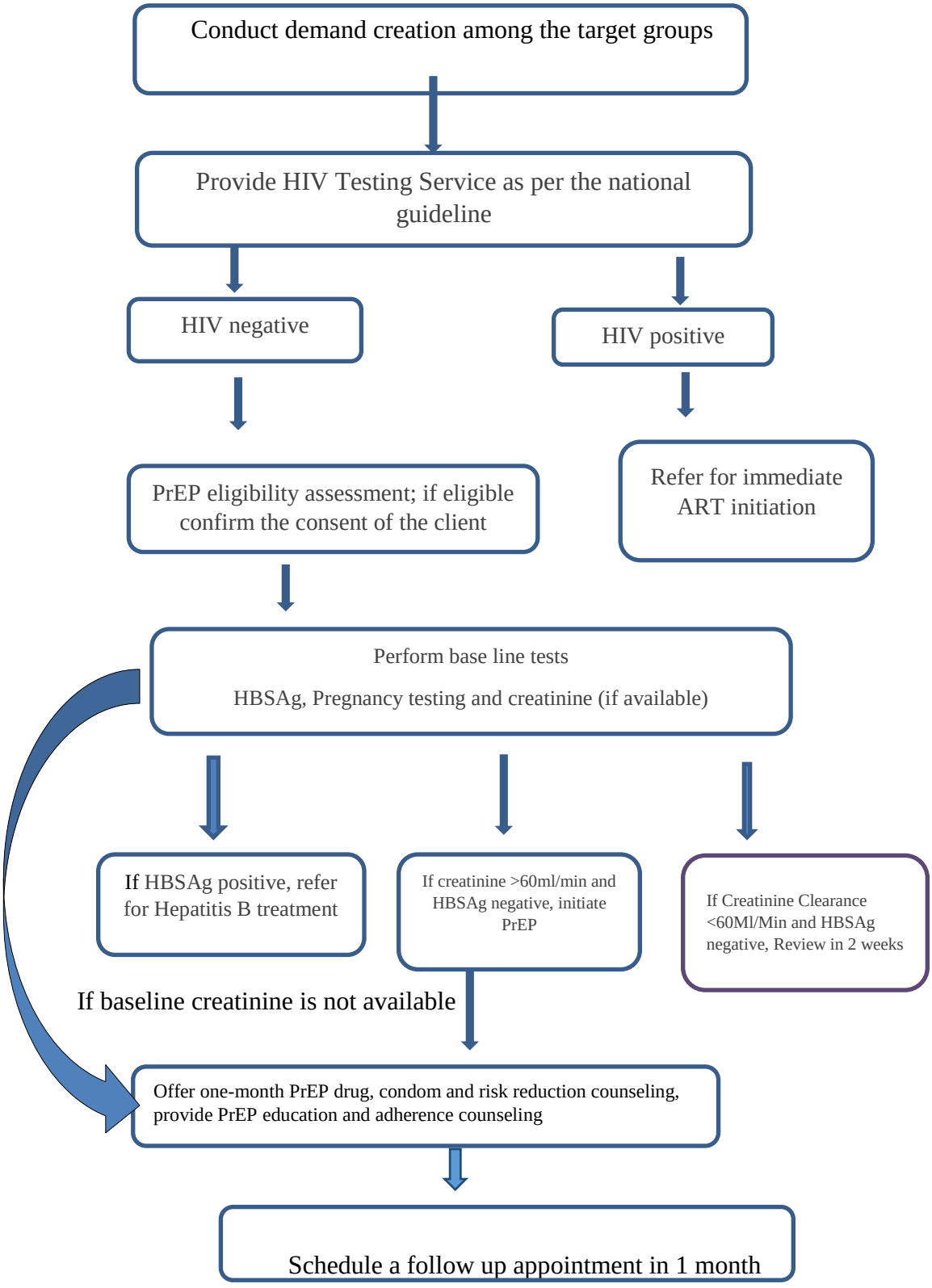
The duration of PrEP use may vary and individuals are likely to start and stop PrEP depending on their risk assessment. Because PrEP is user driven, users have to be provided with the appropriate information on how to stop PrEP to ensure effectiveness. For users who want to stop PrEP, they should have to do so after consulting the health care provider. PrEP medication should be continued for 28 days after the last potential HIV exposure to ensure coverage and protection.

PrEP should be stopped if the client:

- Has a positive HIV test result
- Develops renal disease (refer to the national guideline on comprehensive HIV care and treatment)
- Has become non - adherent to PrEP (i.e. as per the national definition for adherence, poor adherence, non – adherence).
    - If the client misses 5 or more doses during the month, Enhanced Adherence Counseling (EAC) will be offered 2 times (once per each visit monthly). If the client keeps on missing doses, and has poor adherence on three consecutive visits, providers may consider discontinuing PrEP.
- Does not need or want PrEP,
- No longer meets the eligibility criteria/ out of substantial risk
- If there are safety concerns, where the risks of PrEP use outweigh potential benefits.

After discontinuation of PrEP, there should have to be follow - up testing for HIV after a month in order to confirm that the client is still HIV negative.

**Figure: PrEP Screening and Initiation Algorithm**



## XIII. CAPACITY BUILDING, MONITORING AND EVALUATION

For proper monitoring and evaluation of PrEP implementation, the revised registers will be utilized at the service providing facilities and will be reported monthly using the DHIS2. Monitoring and evaluation of the service will be integrated in the existing system such as MDT meeting, catchment area meeting, supportive supervision, program reviews at respective levels. Data on services and outcomes including PrEP uptake, adherence, and retention, as well as HIV testing and STI screening, will be utilized at facility MDT, catchment area meetings and facility supervision checklist.

Data elements that are important for monitoring and improve PrEP service are:

1. Number of target beneficiaries receiving HIV testing
2. Proportion of target beneficiaries that tested negative for HIV
3. Proportion of target beneficiaries testing negative for HIV who receive the eligibility assessment for PrEP
4. Proportion of eligible target beneficiaries who initiate PrEP
5. Proportion of target beneficiaries starting PrEP who are retained at 1, 3 and 6 months after initiation
6. Proportion of target beneficiaries who discontinue PrEP and the main reason:
    a. Among target beneficiaries, proportion who discontinue due to end of substantial risk of HIV
    b. Among target beneficiaries on PrEP, proportion remaining at substantial risk at follow-up but who decide to discontinue for personal reasons
    c. Among target beneficiaries who discontinue PrEP, proportion discontinuing due to side effects
7. Proportion of target beneficiaries who test HIV+ (new sero – conversion) on follow-up visits
8. Proportion of target beneficiaries starting PrEP who complete a repeat test for HIV three months after initiation

Based on the national PrEP training, the regions are expected to cascade the training package to facility ART trained health care providers. The service should be provided by trained ART providers in ART clinic, PMTCT clinic, KP friendly clinics and ART providing DICs. PrEP trained providers will conduct onsite orientation to Pharmacy staffs, Data clerks, case managers, community mobilizers (peer educators/navigators)

## XIV. ROLES AND RESPONSIBILITIES

FMoH:

- Lead the task force on PrEP national implementation and monitoring
- Harmonize the participation of different stake holders for smooth implementation of PrEP scale up
- Provide central training (TOT) on PrEP
- Write a circular letter to RHBs mentioning about cascading of the training, use of the revised working documents (implementation manual, training slides, job aides and client education materials) and reporting through DHIS2
- Share the soft copy of the customized working documents

FHAPCO

- Leadership and coordination of stakeholders on implementation of PrEP
- Demand creation of PrEP service availability and benefits through mass media
- Closely monitor the progress of the implementation,
- Incorporate the implementation of PrEP in its regular supportive supervision and
- Monitoring scheme,

EPSA

- Plan and execute the forecasting and procurement of drugs for PrEP
- Strictly monitor the stock in order to minimize/avoid stock out and wastage of ARVs.
- Avail logistics data timely to stakeholders for decision-making.
- Support facilities for appropriate inventory management, reporting and requisition, and storage.
- Handle emergency orders properly (if any).

Ethiopian Public Health Institute (EPHI)

- Closely follow up and make sure that those facilities have uninterrupted testing services
- with shorter TAT
- Ensure early High viral load result delivery to hospitals
- Generate viral load related report to inform the health program
- Civil Society Organizations including PLHIV associations
- Be actively involved in the implementation of PrEP services
- Advocacy on availability and benefits of PrEP service

RHBs/ZHDs/WoHO

- Write a circular letter to facilities to guide the implementation of PrEP
- Cascade regional and sub-regional level training/orientation
- Monitor the overall of PrEP service implementation including monthly report.
- Coordinate with EPSA to ensure continuous availability of the required supplies
- Ensure the availability and utilization of working documents for PrEP

Health Facilities

- Ensure ART providers received training on PrEP.
- Provide onsite orientation for other staffs by trained ART Providers
- Provide PrEP service to eligible clients as per the guideline
- Facilitate referral and feedback tracking for clients who need transfer to other PrEP service providing sites
- Ensure regular stock status monitoring for all the supplies
- Make sure that clients are properly informed about PrEP benefits
- Discuss PrEP implementation on the MDT and other platforms.
- Ensure client service records properly filled and reported timely using DHIS2
- Request supports from RHBs if there is any need.

Partners

- Provide technical and financial support for scale up of PrEP implementation including demand creation at all levels
- Provide PrEP service including demand creation at ART DICs