

# Summary of Guidelines for the Use of Pre-Exposure Prophylaxis for HIV in Korea

The Korean Society for AIDS

There are several guidelines for the use of pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV) which are used in other countries. However, the implementation of such guidelines in each country should be modified according to the country's clinical and epidemiological situation. Therefore, The Korean Society for AIDS founded a committee in 2016 to develop guidelines for the use of PrEP for HIV that are optimal for Korea's clinical and epidemiological situation. These guidelines aim to provide comprehensive information for PrEP implementation in Korea. The recommendations contain important information for physicians working to prevent HIV infection in actual clinical fields. The committee will regularly review and revise the guidelines based on changes in PrEP administration and HIV prevention practices.

**Key Words:** Human immunodeficiency virus; Preexposure prophylaxis; Prevention; Antiretroviral treatment

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\* The following recommendations are a set of practical guidelines based on the current (August 2017) domestic Korean status. Rather than applying the following principles to the general public, we recommended that the pre-exposure prophylaxis be based upon clinical decision making according to the patient's individual health history.

\* The following recommendations can be used for educational and personal clinical practices, but cannot be utilized for any commercial or clinical evaluation purposes. Those who wish to use the following guidelines for purposes other than educational or personal clinical practice must submit a written form and obtain written consent from the committee.

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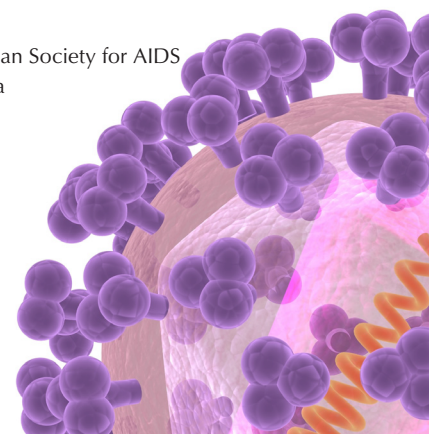
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## Rating scheme for recommendations

Recommendations in these guidelines are based upon scientific evidence and expert opinion. Table 1 shows the rating scheme according to the strength of the recommendation and the quality of the evidence [1].

## Key evidences

The preexposure prophylaxis initiative (iPrEx) study was a randomized, double-blind, placebo-controlled trial conducted among men and male-to-female transgender adults who reported having sexual intercourse with a same sex partner during the 6 months preceding enrollment [2]. Participants were randomly assigned to receive a daily oral dose of either the fixed-dose combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) or a placebo. Enrollment in the TDF/FTC group was associated with a 44% reduction in the risk of HIV acquisition (95% confidence interval [CI], 15-63).

The Partners PrEP trial was a randomized, double-blind, placebo-controlled study of daily oral TDF/FTC or TDF for the prevention of acquisition of HIV by the uninfected partner in 4,758 HIV-serodiscordant heterosexual couples in Uganda and Kenya [3]. The trial was stopped after an interim analysis in mid-2011 showed statistically significant efficacy in the medication groups (TDF/FTC or TDF) compared with the placebo group.

The Bangkok tenofovir study was a randomized, double-blind, placebo-controlled study that assessed the safety and efficacy of daily oral TDF for HIV prevention among 2,413 injection drug users (IDUs) in Bangkok, Thailand [4]. In the modified intent-to-treat analysis (excluding 2 participants with evidence of HIV infection at enrollment), efficacy of TDF was 48.9% (95% CI, 9.6-72.2;  $P = 0.01$ ).

## Recommendations

### 1. Indication of PrEP for HIV prevention in Korea

1. PrEP is recommended as a prevention option for sexually-active men who have sex with other men (MSM) (AI).
2. PrEP is recommended as a prevention option for heterosexually-active women and men whose partners are known to be HIV infected (*i.e.*, HIV serodiscordant couples) (AII).
3. PrEP can be considered an HIV prevention option for injection drug users (CI).

### 2. Preferred antiretroviral regimen for HIV PrEP

1. The recommended regimen for PrEP with all the indicated populations is a daily administration of 300 mg TDF co-formulated with 200 mg FTC (AI).
2. TDF alone can be considered as an alternative regimen for serodiscordant couples and IDUs (CI).

### 3. Dosing recommendation for HIV PrEP

1. The recommended regimen for PrEP with all the indicated populations is a daily administration of 300 mg TDF co-formulated with 200 mg FTC (AI).
2. On demand, PrEP can be considered for high risk MSM (BI). For on-demand PrEP, a loading dose of two pills of TDF-FTC are administered within 24 hours before sex, followed by a third and fourth pill administered 24 and 48 hours after the first dose.

**Table 1.** Strength of recommendation and quality of evidence for recommendation

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement	I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
B: Moderate recommendation for the statement	II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
C: Optional recommendation for the statement	III: Expert opinion

#### 4. Assessment and testing before initiation of PrEP

1. HIV testing and the documentation of results are required to confirm that patients do not have HIV infection when they start taking PrEP medications (AIII). HIV Ag/anti-HIV Ab combo assay should be performed before starting PrEP (AIII). The patient should have a negative result from the HIV Ag/anti-HIV Ab combo assay within one week of PrEP initiation (AIII). The regimen should not be started if the results are inconclusive or if an oral specimen rapid test has been performed. (BIII).
2. Renal function should be evaluated with estimated creatinine clearance (CrCl) before starting TDF/FTC (AIII). TDF/FTC can be prescribed for persons with CrCl  $\geq 60$  ml/min (AIII). Any person with a CrCl of  $<60$  ml/min should not be prescribed PrEP with TDF/FTC (AIII).
3. Testing for hepatitis B virus (HBs Ag, HBs Ab) and hepatitis C virus (HCV Ab) should be performed before starting PrEP (AIII). Hepatitis B virus vaccination is recommended for MSM without HBs Ab (AIII).
4. Acute HIV infection must be excluded by symptom history, physical examinations, and appropriate HIV testing before PrEP is prescribed (AIII).
5. If HIV testing shows intermediate results, clinicians should hold PrEP initiation, make efforts to identify symptoms and signs of acute viral infections, and do follow-up HIV testing (AIII).

#### 5. Clinical follow up and monitoring during PrEP (Table 2)

1. All persons receiving PrEP should be seen at one month following PrEP initiation, and at least every 3 months to assess side effects, adherence, and HIV acquisition risk behaviors (AIII).
2. All persons receiving PrEP should be seen at least every 3 months to assess for signs or symptoms of acute infection and repeat HIV testing (HIV Ag/anti-HIV Ab combo assay). If acute infection is suspected, HIV RNA testing should be performed (AIII).
3. Confirmative HIV testing (western blot assay) and HIV RNA testing should be performed for persons with positive results of screening assay (HIV Ag/anti-HIV Ab assay) (AIII). Resistance testing should be performed for persons with confirmed HIV infection during PrEP (AIII).

4. If acute HIV infection is suspected during PrEP, PrEP should be stopped, and combination antiretroviral therapy with TDF/FTC + boosted protease inhibitor (darunavir/ritonavir) or TDF/FTC + dolutegravir should be prescribed (AIII).
5. Women who may become pregnant should be seen at least every 3 months to repeat pregnancy testing during PrEP (AIII).
6. All persons receiving PrEP should be seen at least every 3 months to monitor CrCl (AIII).
7. Sexually active persons receiving PrEP should be seen at least every 6 months to conduct tests for sexually transmitted infections (*i.e.*, syphilis, gonorrhea, chlamydia) (BII).
8. Assessment of bone health is not routinely recommended before the initiation of PrEP or for the monitoring of persons while taking PrEP (BI). However, assessment for bone health can be considered for any person who has a history of pathologic fractures or who has significant risk factors for osteoporosis.
9. All persons receiving PrEP should be seen at least once every 12 months to evaluate the need to continue PrEP as a component of HIV prevention considering HIV acquisition risk behavior, PrEP adherence, and other factors (BIII).

#### 6. Education for persons taking PrEP

1. Clinicians must educate persons taking PrEP about the importance of adherence (AIII).
2. Clinicians must educate persons taking PrEP to reduce HIV risk behaviors (AIII).

**Table 2.** Clinical follow-up and monitoring for HIV-uninfected person taking PrEP

Intervals	Assessment
3 months	Side effects, adherence, HIV acquisition risk behaviors HIV screening testing (HIV Ag/anti-HIV Ab combo assay) Pregnancy testing
6 months	Estimated creatinine clearance Testing for sexually transmitted diseases (syphilis, gonorrhea, chlamydia, <i>etc.</i> )
Optional	Bone mineral density Therapeutic drug monitoring

HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis; Ag, antigen; Ab, antibody

## Conflicts of Interest

No conflicts of interest.

## Supplementary material

Guideline Korean version.

Supplementary data can be found with this article online <http://www.icjournal.org/src/sm/ic-49-243-s001.pdf>.

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