What's new in the Belgian PrEP ~~guidelines~~?

Jens Van Praet, MD PhD

AZ Sint-Jan, Brugge

11th BREACH Symposium – Dolce La Hulpe

30/11/2023

Background

- At the introduction of PrEP in Belgium ‘Use of Pre Exposure Prophylaxis (PrEP) : Belgian guidelines’ was developped
  - Presented at a College of the HRCs meeting and shared among HRCs
- 28/03/2022: proposal for update of Belgian guidelines in PrEP network meeting
- Working group:

Gert Scheerder (ITG)

Anne Vincent (UCL Saint-Luc)

Anne-Sophie Sauvage (CHU Liège)

Sophie Henrard (Erasme)

Jens Van Praet (AZ Sint-Jan)

Agnès Libois (Saint-Pierre)

Chris Kenyon (HRC Antwerpen)

Annelies Meuwissen (UZ Brussel)

Jef Van Hamel (ITG)

Henrard S *et al*, 2017

Update of Belgian PrEP ~~guidelines~~

- New evidence has emerged since the start in 2017
- A study performed by the ITM indicated differences across HRCs in the content of PrEP care provided:
  - Timing of PrEP initiation
  - Frequency of follow-up consultations
  - STI screening policy
  - …
- Care for PrEP users has shifted partially from the HRC to first line healthcare
  - As of July 2023, 2 visits per year can be organized by the GP according to the reimbursement criteria

HRC: HIV Reference Center, GP: general practitioner

Vanhamel J et al, 2022

‘Guidelines’ of ‘guidance’: What's in a name?

Guidelines	Guidance
The evidence must be searched and evaluated systematically	More narrowly focused document for areas where data continue to rapidly evolve
The team working on the guideline should be a multidisciplinary panel of experts and representatives	Prepared by a small team of experts
Patient groups and patient preferences must be considered	Based on a comprehensive (but not necessarily systematic) review of the literature, clinical experience, and expert opinion
The process should be explicit and transparent	Do not include formal grading of evidence, and are made available online
The guideline should be reconsidered and revised when important new evidence warrants modifications	Updated annually

Guyatt GH et al, 2008; Tamma PD et al, 2023

Belgian PrEP guidance: table of contents

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PEP: post-exposure prophylaxis; STI: sexually transmitted infection

PrEP eligibility

To judge eligibility for PrEP, we advise health care providers to perform an individualized risk-benefit assessment based on a detailed sexual and drug use history. PrEP should be considered in HIV negative patients older than 16 years at high risk of acquiring HIV. These patients include:

1. Men having sex with men and transgender individuals at high risk of acquiring HIV
    a. Reporting unprotected anal sex with one or more partners in the last 6 months
    b. Acquisition of multiple STI during the last year, including syphilis, chlamydia, gonorrhea, or acute hepatitis B or C
    c. Use of psychotropic substances during sexual activity (Chemsex)
    d. Treatment with HIV post-exposure prophylaxis in the last year
2. Other persons with a high individual risk
    a. People who inject drugs sharing needles
    b. Sex workers exposed to unprotected sex, particularly anal sex
    c. People exposed to unprotected sexual activities, at high risk of HIV acquisition*
    d. Sexual partners of a seropositive individual with a detectable viral load

** These include persons originating from a country with a high HIV prevalence (e.g., in sub-Saharan Africa) visiting regularly their country of origin and heterosexual women who engage in unprotected sex with male partners who are at high risk of HIV acquisition (e.g. bisexual male partners or male partners from areas with a high prevalence).*

In patients with **chronic kidney disease stage 3 or higher** (estimated glomerular filtration rate <60 mL/min/1.73 m^2) the initiation of event driven PrEP (emtricitabine/tenofovir disoproxil (FTC/TDF)) can be considered if the benefit is deemed higher than the risk of progressive kidney disease. When suspecting an acute HIV infection or in patients with a doubtful recent HIV test result, we advise to defer the start of PrEP with 4 weeks and perform a second HIV test. Patients who are eligible for PrEP commencement based on these criteria should be referred to HRC.

HIV is not transmissible through sexual contacts with partners living with HIV who have an undetectable viral load, and thus PrEP is not indicated in these cases.

FTC: emtricitabine; TDF: tenofovir disoproxil fumarate

Special situations

- Woman who are pregnant or trying to conceive
  - Offer PrEP to women whose partner has HIV, especially when their current partner's viral load is unknown, is detectable, or cannot be documented as undetectable
- Breastfeeding
- Chronic hepatitis B infection
  - Do not use event driven PrEP
  - Monitor for hepatitis flares if PrEP is discontinued
- Recent PEP exposure - Switching directly from PEP to PrEP
  - PrEP can be started directly after PEP if indicated
- Transgender persons
  - Event driven PrEP should not be offered, unless they are exclusively having anal sex
- Bariatric surgery
  - TDF plasma concentration may be lower than expected
  - Need for closer follow-up and encouragement to adhere to other recommended prophylactic measures

Initial assessment and follow-up

- First medical consultation
  - Attention should be given to symptoms of an acute HIV infection (perform HIV-PCR even if HIV test is negative or second HIV test 4 weeks later)
  - If there are no signs or symptoms of recent seroconversion, PrEP can be started as soon as contraindications have been ruled out: offer prescription that can be used 48h later
- First follow-up consultation
  - At 1 month in case of recent risk of HIV acquisition before starting PrEP or risk of misunderstanding of PrEP usage
  - Discuss immunization against hepatitis A and B, Mpox, meningitis B and HPV (for patients under 40 years)

HPV: human papillomavirus

Three months follow-up consultations

	After 1 month (optional)	3 monthly	6 monthly	12 monthly
HIV 4th generation test	x	x		
Syphilis		x		
ALT/GPT		x		
HCV			x	
Serum creatinine, eGFR and serum phosphate*	x			x
Urine protein/creatinine ratio*				x

- *More frequent screenings (3-6 monthly) should be considered in individuals over 50 years of age, with CKD or risk factors for CKD (e.g. diabetes and hypertension) or who use of nephrotoxic medications. Preferably these patients are followed up in an HRC
- We recommend only testing MSM for NG or CT if:
  - they have symptoms compatible with these infections or a partner has a symptomatic infection
  - they have sex with women as well as men
  - they express a strong desire for asymptomatic screening
- For women, transmen and men who have sex with women, NG/CT should be tested intermittently according to risk.

NG: *N. gonorrhoe;* CT: *Chlamydia trachomatis;* ALT/GPT: Alanine Amino Transferase

PrEP counseling: key components

- **Risk reduction**
  - Assess the risk: type of sexual intercourse, use of alcohol/chem sex, condom use, use of sextoys and discuss risk reduction
  - Chemsex: educate for individual tools, interactions between drugs (see chemsex.be, application knowdrugs)
  - Review STI transmission mode (refer to O'YES.be)
  - Reinforce the need for immunization (e.g. HPV and hepatitis)
  - Assess potential sexual dysfunction: discuss the role of chemsex and mental health. Refer to sexologist, mental health specialist, addiction specialist or community associations if needed.

- **Educate for STI screening when symptoms are present and partner notification**

- **Medication adherence**
  - Test the understanding of the chosen regimen of PrEP: real life case study
  - Provide pill box, mobile applications and websites
  - Discuss strategies to adopt in case of discontinuation: out of stock situation, unexpected travel, …
  - Discuss the indication of PEP
  - Ensure availability of the care givers: offer a list with telephone numbers, e-mail addresses and emergency hotline

PrEP regimen and dosage

Population	Starting oral PrEP	Using oral PrEP	Stopping oral PrEP
Cisgender men and trans and gender diverse people assigned male at birth who 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 1 dose per day	Take 1 dose per day until 2 days after the day of the last potential sexual exposure**
Cisgender women and trans and gender diverse people assigned female at birth*	Take 1 dose daily for 7 days before potential exposure	Take 1 dose per day	Take 1 dose daily for 7 days after last potential exposure
Cisgender men and trans and gender diverse people assigned male at birth who are taking exogenous estradiol-based hormones*	Take 1 dose daily for 7 days before potential exposure	Take 1 dose per day	Take 1 dose daily for 7 days after last potential exposure
People using oral PrEP to prevent HIV acquisition from injecting practices*	Take 1 dose daily for 7 days before potential exposure	Take 1 dose per day	Take 1 dose daily for 7 days after last potential exposure

* patients in need of chronic hepatitis B treatment should take daily PrEP. Stopping PrEP should be discussed with physician and monitoring is recommended after stopping TDF-based PrEP to detect relapse and manage HBV.
** Some event-driven PrEP studies (2) showed effectiveness by taking 2 doses daily after potential exposure, even if the first of the 2 last doses is on the same day of the last exposure for it is after the exposure. Sources like WHO recommend taking 2 daily doses after the last potential exposure.

Missed medication and indications for PEP

- If a person forgot to take his pill within 12 hours, the next pill should be taken as soon as possible, and PrEP continued at the same hour as usual. If a person forgot to take his pill later than 12 hours, only the next pill should be taken at the same hour as usual.
- In case of a risk contact and suboptimal medication adherence, the HRC should be contacted to evaluate the need for PEP. Low adherence is defined as:
  - For men and women on daily regimen: less than 4 pills a week, regardless of the distribution
  - For men taken even-driven PrEP: less than 1 pill before and 1 pill after sexual intercourse

Side effects

- Gastrointestinal symptoms
- General symptoms
- Renal failure: One-time elevations in serum creatinine are seen in approximately 1 in every 200 PrEP users but are self-limiting and resolve in 80% of cases without stopping PrEP when a separate specimen is tested. The Fanconi syndrome is a seldom side effect of TDF usage. In patients with worsening of kidney function, we proposed to confirm this on a separate specimen. If creatinine clearance drops below <60mL/min, we advise to refer the patient to the HRC. Also, if creatinine clearance decrease over 20% without recovery, the patients should be referred the to HRC for further work-up including determination of urinary protein/creatinine ratio, glucosuria, fractional phosphate excretion, measurement of urine pH and plasma bicarbonate.
- Reduction of bone density

Other topics

- Seroconversion and resistance
  - Perform drug resistance testing should be performed before starting treatment
- Doxycycline to prevent STIs
  - No statement was made
- Patient information
    - Main messages
    - Websites: Myprep.be, Sensoa, PrEPster and PROMISE
- Information to be collected by the HRCs

1. The number of individuals starting PrEP in the last year, including their sex, age group, risk category, presence of specific circumstances (sex work and start after PEP usage) and regimen chosen at the start.

2. The number of individuals taking PrEP in the last year, including the number with a new diagnosis of a specific STI (HIV, syphilis, NG, CT, LGV, hepatitis A, hepatitis B, hepatitis C, Mpox and HIV), the number reporting chemsex usage and the regimen at the last consultation of the year.

3. The number of individuals who interrupted PrEP and the reasons for this interruption.

LGV: lymphogranuloma venereum

Wrap-up

- The ‘Belgian Guidance on the use of Pre-Exposure Prophylaxis’ is a non-normative document providing a point of reference for standard PrEP care in Belgium
- A first version composed by a writing group will be sent to all HRC for endorsement
- A final version will be published and reviewed on regular basis by the working group