



NOTE

Recommendations regarding commissioning of PrEP

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The recommendations have been prepared by the working group for commissioning of PrEP, which was appointed by the regions via health director e-mail no. 40/2018. The recommendations were approved by the Danish Regions' Health Committee 31. January 2019.

The terms of reference of the working group, as well as the composition, appear from the attached appendices.

Background

In September 2018, the National Board of Health published a recommendation that the regions should offer PrEP as a preventive treatment offer against HIV of up to 500 people annually in special risk groups. The treatment initiative is a pharmacological supplement to the existing prevention efforts, which must continue to focus on safe sex, early detection and effective treatment. It is the Danish Health and Medicines Authority's assessment that one can expect a significant decrease in the number of newly infected, perhaps up to a halving.

The Danish Medicines Agency has stipulated that dispensing of medicine must take place from the hospitals' infectious medicine departments.

On the basis of the Danish Health and Medicines Authority's recommendation, the circle of health directors decided on 26 October 2018 that an interregional working group should be set up to prepare a strategy for the introduction of PrEP as preventive treatment against HIV by people in special risk groups.

The terms of reference for the working group state that the working group must concretely prepare a common regional guide for target group delimitation, extradition practices and control follow-up. The working group will also look at a strategy for what are the options in the longer term with a focus on practical implementation in the outpatient clinics. This with a LEON mindset in mind (lowest effective cost level).

The Region of Southern Denmark has chaired the working group. The working group must report to the regions' health directors.

Appendix 1 sets out the terms of reference of the working group. Appendix 2 shows the composition of the working group. Appendix 3 shows the extent to which the regions today

offers PrEP treatment as well as the prices of the various medicinal preparations.

Overall recommendations from the working group:

- That the regions offer treatment of up to 500 patients on an annual basis
 - and the number is exclusive of the more than 200 patients currently treated with PrEP.

- That treatment with PrEP, in the framework outlined in this report, runs for 1 year, after which an evaluation and collection is made with a view to adjustment etc. of the recommendations. This i.a. with regard to reassessing the target group etc ..

- That the treatment of the patient group also continues during the evaluation is ongoing. Thus, it is not the working group's expectation that patients who have started PrEP treatment should stop this. This will always be a decision to be made under the auspices of the health director circle and politically.

- That it is ensured that all treatment sites use the diagnosis code DZ298 for the group of patients receiving PrEP treatment.

- That a quality database is established for PrEP, e.g. in order to monitor the quality of the treatment and form the basis for an evaluation of the recommendations in 1 year. It must be investigated further whether the database is to be anchored under the auspices of RKKP or in a responsible hospital ward. It is estimated that it will cost DKK 100,000 - 200,000 to establish the database under the auspices of RKKP. In addition, there are expenses for operating the database. It is unknown what the establishment of a database on a responsible hospital ward will cost.

In relation to TARGET GROUP, the following is recommended:

The target group for the preventive treatment are people who, based on a number of objective criteria, are at high risk of becoming infected with HIV.

It is recommended that PrEP be given to individuals who meet all of the following criteria:

1. The person is HIV-negative

2. The person belongs to the group of men who have sex with men or the group of trans women or trans men who have sex with men, and meets at least 1 of the following criteria:

- The person has had unprotected anal intercourse with at least 2 male partners within the last 12 weeks ¹
- The person has had syphilis within the last 24 weeks
- The person has had chlamydia or gonorrhea within the last 24 weeks

3. The person is 18 years old or older

4. The person has normal renal function (eGFR- ≥ 60 mL / min.)

5. The person has acceptable liver and bone marrow function:

- TOTAL ≤ 2.5 x upper normal limit
- Neutrophils ≥ 1000 / mm ³
- Platelets $\geq 75,000$ mm ³
- Hemoglobin ≥ 6 mmol / l

6. The person must be willing to follow the applicable guidelines in relation to the treatment

It is recommended that the treatment site continuously assess whether there is still a need for the patient to be treated with PrEP, and that treatment be stopped in the event that the patient is no longer in the high-risk group of becoming infected with HIV.

In relation to the ORGANIZATION OF THE TREATMENT AT THE HOSPITALS, the following is recommended:

- The treatment must be handled by a specialist in infectious disease, or on delegation from this.
- Treatment with PrEP is covered by the Danish Health and Medicines Authority's current specialty plan, and will only be able to be handled within the same approvals as currently apply for handling PEP treatment. Currently, the following infectious disease departments are approved for PEP treatment:

- Rigshospitalet
- Herlev
- Hvidovre
- Hillerød
- Roskilde
- Odense
- Aarhus University Hospital

¹ A well-known HIV-negative partner does not count

- Herning
 - Aalborg
- It is recommended that the individual region assesses the possibilities for the treatment offer to be organized as an outgoing function from the infectious disease hospital ward, e.g. in collaboration with clinics for sexually transmitted diseases, NGO-driven "checkpoints" for HIV testing mm.

In relation to SCREENING BEFORE IMPLEMENTING PREP, the following is recommended:

Prior to treatment with PrEP, it is recommended that hospitals perform the following:

- HIV test (antibody / p-24 antigen combo test)
- Survey for:
 - island Hepatitis A + B + C
 - island Syphilis
 - island Chlamydia (urethra, pharynx and rectum)
 - island Gonorrhea (urethra, pharynx and rectum)
- Biomarker studies (blood test): Hematology, liver count and kidney fluid count
- In case of negative Hepatitis A and / or B serology, vaccination should be offered
- Patients who are Hepatitis B positive are also offered treatment with PrEP, but it is emphasized that treatment with PrEP will only be stopped if this has been agreed with a doctor, as there is a risk that the virus will flare up.

In relation to CONTROL FOLLOW-UP AND DELIVERY PRACTICE, the following is recommended:

That everyone who is offered PrEP treatment:

- First have a 4 week period where they have safe sex before PrEP is handed out. The agreement on the waiting period of 4 weeks can be agreed with the patient without attending the hospital
- After the 4 weeks, the person must show up physically at the hospital and have undergone an HIV test. This in order to ensure that persons there

starts PrEP treatment, is not infected with HIV before starting treatment.

- If the HIV test is negative, the person will be given medication for 3 months' consumption with information about:

- island How to take the medicine

- island Side effects of the medicine

- island The importance of compliance with prescribed pill intakes for shooting effect

- island The importance of using a condom that also protects against others sexually transmitted diseases - PrEP does not

- 4 weeks after the start of treatment, there must be a virtual meeting (eg telephone conversation) between doctor and patient, among other things. with follow-up on how the medicine is taken, whether the person experiences side effects etc.
- Thereafter, the person must appear every 3 months at the infectious disease outpatient clinic where the following must be performed:

- island HIV test (antibody / p-24 antigen combo test) NAT test

- island (not mandatory)

- island Blood tests to monitor kidney function Syphilis test

- island

- island Screening for chlamydia and gonorrhea from

- Rectum (inoculation)
 - Swallow (inoculation)
 - Urethra (urine sample)

- island Samta le in order to ensure proper use of the prescribed medication and in order to assess continued indication for PrEP

- Therefore, hepatitis A, B and C are tested every 6 months in relation to the following:
 - island anti-HAV and HBs antigen in previously uninfected and non-vaccinated down
 - island anti-HCV in previously uninfected
 - island HBV DNA in individuals with positive HBs antigen

- If the examinations show that there is a need for treatment, the hospital is responsible for the treatment.

In relation to MEDICINE, the following is recommended:

- That medication is prescribed for a maximum of 3 months at a time.
- That medication is only dispensed for the first time if the person has practiced sexual intercourse with a condom for the previous 4 weeks or has not had sexual contact at all, and the subsequent HIV test is negative.
- It is recommended that a generic tenofovir / emtriciabine be used for a 1-year trial period, e.g. from Mylan. It will cost the regions a total of DKK 6.3 million. DKK annually for the treatment of 500 people (excluding expenses for follow-up visits, tests, vaccinations and possible treatment). Alternatively, the combination preparations with tenofovir disoproxil + lamivudine can be used if there is a desire to reduce the cost. As this solution requires the person to take 2 pills, there is a greater risk of poor adhesion. The price of the various medicinal products is set out in Annex 3.
- It is recommended that PrEP be taken as a daily dose (and thus recommended) **does not**, that the pill is taken "on demand", as there is a risk of greater negative compliance).

Prices for PrEP treatment

Cf. the table below is the estimated cost of treatment with PrEP for 1 year approx. 12.5 million
The cost of blood tests and initiation of treatment in the event of positive findings of e.g. chlamydia, syphilis mm.

Table 2: Expenditure on treatment with PrEP

Performance	Price in kr.	Total price at treatment of 500 per-zone pr. year
Treatment with Mylan	12,600	6,300,000
Start-up visit		
HIV test (antibody / p-24 antigen combo test)	32	16,000
Hepatitis A + B + C	232	116,000
Syphilis	64	32,000
Chlamydia (urethra, esophagus)	891	445,500
Gonorrhea (urethra, pharynx)	891	445,500
Vaccination mode Hepatitis A + B (Twinrix)	1,638	163,800
Biomarkers (blood tests): hematology, liver count, kidney fluid count	Unknown	Unknown
Specialist medical resource estimated 40min.	416 kr.	208,000
Follow-up visits (4 times a year per patient)		
HIV antibody / p24 antigen test	32	64,000
Hepatitis A + B + C (2 x annually) NAT	232	232,000
test	147	294,000
Blood tests to monitor adverse reactions (renal fluid counts) Unknown		Unknown
Chlamydia (urethra, esophagus)	891	1,782,000
Gonorrhea (urethra, pharynx)	891	1,782,000
Specialist medical resources 20.min pr. follow-up visits	208	416,000
Nursing Resources 20.min pr. follow-up visits	99	198,000
Total		12,494,800