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Govern d'Andorra

PROTOCOL FOR PRESCRIBING AND MONITORING HIV PRE-EXPOSURE PROPHYLAXIS (PrEP)

Ministry of Health

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PROTOCOL ELABORAT PER L'ÀREA DE RECURSOS SANITARIS.

PROTOCOL APROVAT PEL CONSELL ASSESSOR SOBRE LA PATOLOGIA INFECCIOSA EN DATA 11-05-2023.

USE OF HIV PRE-EXPOSURE PROPHYLAXIS (PrEP)

I. INTRODUCTION

PrEP (pre-exposure prophylaxis) is treatment with antiretroviral drugs to prevent infection by HIV (Human Immunodeficiency Virus). The inclusion in the portfolio of services of the new indication of the combination is a tool to prevent HIV infection.

Treatment should be accompanied by recommendations and additional interventions focused on reducing risk behaviour, adopting healthy behaviours and early detection of HIV infection or other sexually transmitted infections (STIs):

- Condom use
- Update on vaccination status (hepatitis A and B)
- Early diagnosis and treatment of HIV infection
- Early detection and treatment of other STIs
- Sex Education and Assisted Counseling
- Assessment of intentional drug use during sexual intercourse (*Chemsex* - chemical sex)

Decree 505/2022, of 30-11-2022, establishes the criteria and conditions for the reimbursement, by the Caixa Andorra de Seguretat Social, of medicines containing emtricitabine 245 mg and tenofovir disoproxil fumarate 200 mg as pre-exposure prophylaxis of HIV infection. The objective of **preventive treatment** is to reduce the likelihood of contagion of sexually acquired HIV infection by high-risk behaviors, following the regimen of continuous administration (1 tablet / day).

Control and monitoring of the PrEP user population is essential, since incorrect use can lead not only to HIV infection, but also to develop resistance to antivirals or unwanted clinical complications. For this reason, this protocol is established, which will define guidelines on the dispensing, control and monitoring of PrEP users to ensure the effectiveness of the intervention.

The protocol aims to identify the minimum criteria that must be met for the start, the Control and monitoring, and withdrawal criteria.

Prescription criteria for PrEP

Be over sixteen years old and meet any of the following criteria:

a) Present at least two of the following circumstances in the last twelve months:

- Have had more than ten sexual partners.
- Practice unprotected anal sex.
- Administration of post-exposure prophylaxis to HIV on different occasions.
- Having had an episode of sexually transmitted infection of bacterial origin.
- Use of drugs during sexual intercourse.

b) Be a person in a situation of vulnerability exposed to unprotected sexual relations.

c) Other situations that may be considered high risk of contracting HIV.

Clinical management begins with the referral of the referring doctor to internal medicine with the reason for referral "PrEP treatment". The patient is treated in the hospital's infectious diseases unit and management consists of several phases:

I. First consultation: evaluation of the patient as a candidate to receive PrEP

II. Second consultation: prescription of PrEP *(three weeks later)*

III. Third consultation: control of adherence and adverse effects, plus analytical determination if necessary *(four weeks later)*

IV. Fourth consultation: clinical follow-up and renewal of treatment (*four months later)*

I. First consultation: evaluation of the patient as a candidate to receive PrEP

Before prescribing PrEP treatment, the internist with experience in HIV management should carry out the appropriate personal assessment and analytical determinations.

Personal assessment of the candidate (clinical interview)

- Evaluation of the risk of sexual acquisition of HIV from uninfected patients.
- Search for clinical symptoms compatible with a viral infection.
- Questionnaire on drug use and the practice of chemical sex (*Chemsex*).
- Review of the patient's vaccination status.
- Vaccination against hepatitis A virus (HBV) and hepatitis B (HBV) and against human papillomavirus (HPV), if applicable (with complete regimen by age).
- Identification in the patient of the criteria for receiving PrEP.
- The patient must be informed of:
  - The obligation to comply with medical monitoring in order to receive treatment.
  - The importance of good adherence to treatment to achieve The desired effectiveness, in the regime of continuous administration.
  - Clinical contraindications for the administration of treatment. It includes a review of your usual pharmacological treatment with PrEP through: https://www.hiv-druginteractions.org/checker.
  - The adverse effects that may appear.
  - The importance of reducing risky sexual behaviors and encouraging the use of barrier methods, given that PrEP does not prevent other sexually transmitted infections (STIs).
  - Data currently available on the utilization of emtricitabine / tenofovir disoproxil in the course of pregnancy.
- A contraceptive method should be prescribed, if applicable.

If evidence of recent exposure to HIV-1 is detected, the initiation of PrEP should be

Postponed for a month.

Analytical determination
○ HIV-1 research test *(if the patient shows signs or symptoms, confirmatory tests will be done, in addition to plasma viral load, CVP)* ○ Sexually transmitted infections (STIs) screenings (*see Table 1):* • Syphilis • Gonorrhea • Chlamydia • Hepatitis B (HBV) • Hepatitis C (HCV) • Hepatitis A (HAV) ○ Evaluation of renal function: • Estimated glomerular filtering • Serum creatinine • Serum phosphates ○ Systematic analysis of urine: • Pregnancy test, if applicable • Glycosuria • Sediment • Protein/creatinine ratio in urine

Table 1. Diagnostic techniques for screening for each STI

Diagnostic technique for screening each sexually transmitted infection (STI)		
Infection	**Sample type**	**Technique to use**
HIV	Blood	4th generation ELISA test + Western-Blot confirmation test
HCV	Blood	Anti HCV serology
HBV	Blood	Anti HBs*, anti HBc and HBsAg serology
VHA	Blood	Anti VHA Serology IgG + IgM
Clamydia trachomatis	Urethral secretion or endocervical sample Other risk locations must be assessed: pharynx, rectal... Urine	Culture or PCR or immunofluorescence
Treponema pallidum	Blood	Treponemic Test + Non-Treponemic Test (RPR)
Neisseria gonorrhoeae	Urethral secretion or endocervical sample Other risk locations must be assessed: pharynx, rectal... Urine	Optical microscopy, culture or multiplex PCR (gonococcus/chlamydia)
Trichomonas vaginalis	Women: endocervical or vaginal exudate Men: urethral exudate	Only if there is a clinic of urethritis Optical microscopy and PCR

***HBs:** Hemoglobin S; **HBc:** Hemoglobin C; **HBsAg:** hepatitis B surface antigen*

Screening for other STIs such as *Mycoplasma genitalium* or herpes simplex virus is not routinely recommended according to clinical guidelines. Screening for human papillomavirus (HPV) infection is also not routinely recommended, although HPV vaccination in MSM (men who have sex with other men) under the age of 26 is recommended, as well as screening for cervical and anal dysplasia in some populations.

Administration of emtricitabine / tenofovir disoproxil as pre-exposure prophylaxis is not recommended in:

- Adults with a ClCr < 60 ml/min
- Adolescents with a ClCr < 90 ml/min

II. Second consultation: prescription of PrEP

Three weeks after the first visit and after ruling out HIV infection, the patient returns to start prescribing PrEP.

Personal assessment of the candidate (clinical interview)

- It is necessary to ensure that there has been no recent exposure, subsequent to the analyses carried out. If so, it could delay prescribing with a new check on HIV serology.
- The patient should be informed again of the importance of reducing risky sexual behaviors and should receive appropriate advice.
- Understanding of how treatment works, its risks and benefits and the importance of correct adherence must be confirmed.

- It is necessary to determine the suitability of the treatment, taking into account the results of analytical determinations, making an assessment of the benefit and risk.
- Complementary strategies for harm reduction should be reported.
- It is necessary to provide treatment, information and follow-up, in case of diagnosis
  of an STI.
- Information must be given on the beginning of protection of treatment and the effectiveness of the daily regimen (the latter is 99%).
- The patient should be sensitized about:
  - The importance of knowing your status against the virus through regular monitoring.
  - The extent of not taking the drug on a daily basis.
  - The application of barrier protection measures during the period of initiation to PrEP, to cover the time interval of start of optimal protective efficacy of treatment.
  - The importance of quickly notifying the prescriber to any sign or symptom characteristic of primary HIV-1 infection.
  - The data currently available on the use of Emtricitabine / tenofovir disoproxil in the course of pregnancy.
- A contraceptive method should be prescribed, if applicable.
- It is necessary to indicate the date of the next visit and the dates of the next tests
  Analytical.

- You must submit a brochure indicating the most important data of the treatment.
- It is necessary to prescribe PrEP and inform that the refund will be made Only if it is dispensed from the hospital pharmacy.

Analytical determination

- Evaluation of renal function:
  - Estimated glomerular filtering
  - Serum creatinine
  - Serum phosphates
- Systematic analysis of urine:
  - Pregnancy test, if applicable
  - Glycosuria
  - Sediment
  - Protein/creatinine ratio in urine

III. Third consultation: control of adherence and adverse effects

It will be done four weeks after starting treatment. The prescriber, in the previous consultation, will decide if the third only takes into account the personal assessment, made in the Pharmacy Service of the Hospital Nostra Senyora de Meritxell, or if it also includes the analytical determination made by the same prescriber.

Personal assessment (clinical interview)

- Identification of adverse effects arising and particular situations (pregnancy, misuse and overdoses).
- Examination of the observations reported by the patient for signs or symptoms compatible with acute HIV infection.
- Review of adherence to treatment.
- It is necessary to estimate the patient's understanding of the importance of a good follow-up

  and adherence to treatment to achieve effectiveness.
- The date of the next visit and the dates of the next analytical tests must be indicated.

Analytical determination *(if applicable)*

- HIV-1 serology
- Evaluation of renal function:
  - Estimated glomerular filtering
  - Serum creatinine
  - Serum phosphates
- Systematic analysis of urine:
  - Pregnancy test, if applicable
  - Glycosuria
  - Sediment
  - Protein/creatinine ratio in urine

Kidney monitoring:

- Adults: if the rate of serum phosphates ισ < 1.5 mg/dl (0.48 mmol/l) or if the ClCr is < 60 ml/min, the evaluation of renal function should be repeated within a week and glycemia, kalemia and glycosuria should be added.
- Adolescents: If the rate of serum phosphates is < 3.0 mg/dL (0.96 mmol/l), renal function assessment should be repeated within a week and glycemia, kalemia and glycosuria should be added.

Discontinuation of treatment with PrEP should be considered in patients presenting:

- ClCr < 60 ml/min (in two consecutive analyses).
- Serum phosphate rate < 1.0mg/dL (0.32 mmol/l) (in two consecutive analyses).
- Progressive degradation of renal function without any other apparent cause identified.

IV. Fourth consultation: clinical follow-up and renewal of treatment

Before renewing the prescription for PrEP treatment, between three and four months after the prescription, the internist must carry out the personal assessment and the relevant analytical determinations.

Personal assessment (clinical interview)
○ Identification of adverse effects arising and particular situations (pregnancy, misuse and overdoses). ○ Exploration of the observations reported by the patient. ○ Review of adherence to treatment. ○ It is necessary to estimate the patient's understanding of the importance of a good follow-up and adherence to treatment to achieve effectiveness. ○ PrEP must be prescribed (seroconversion results are required to renew the prescription). ○ It is necessary to indicate the date of the next visit and the dates of the next tests Analytical.
Analytical determination
○ HIV-1 serology ○ Evaluation of renal function: • Estimated glomerular filtering • Serum creatinine • Serum phosphates ○ Systematic analysis of urine: • Pregnancy test, if applicable • Glycosuria • Sediment • Protein/creatinine ratio in urine