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# PREP ACCESS IN EUROPE

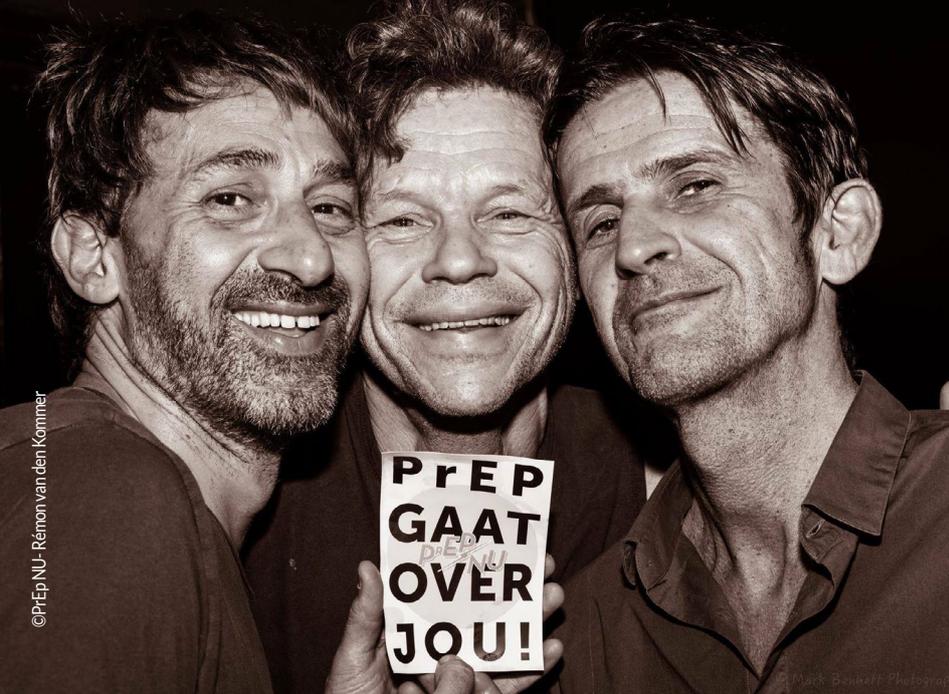


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## PrEP in Europe Initiative (PEI)



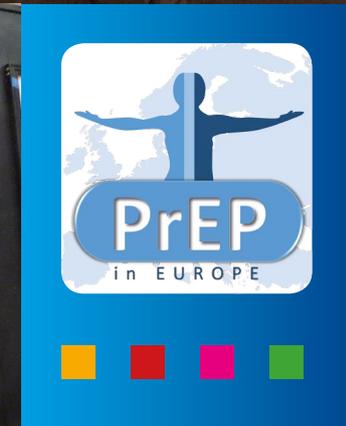
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## About the PrEP in Europe Initiative

The PrEP in Europe Initiative (PEI) is a new initiative, a coalition of European organisations and activists concerned with HIV prevention and specifically with ensuring access to PrEP (pre-exposure prophylaxis) among people at high risk of HIV.

Our mission is threefold: to disseminate up-to-date information on PrEP access in Europe; to influence policymakers and health funders to adopt PrEP in their countries; and to support organisations, groups and individuals advocating for PrEP in their own countries and communities.

It is run by a steering committee of pan-European advocacy organisations including AVAC, NAM/aidsmap, EATG, AIDS Action Europe, the National AIDS Trust and AIDES.

PEI is in the process of establishing a permanent secretariat and website, and it has its own [social media page on Facebook](#).<sup>1</sup>



<sup>1</sup> [www.facebook.com/groups/PrEPinEurope/](http://www.facebook.com/groups/PrEPinEurope/)

## Introduction

PrEP (pre-exposure prophylaxis) refers to the use of antiretroviral medication before exposure (daily or intermittently) by people at risk of HIV to prevent them from acquiring HIV.

In 2015, the World Health Organization (WHO) released new guidelines on HIV prevention, diagnosis, treatment and care for key populations stating that PrEP was recommended as a prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches.<sup>2</sup>

The US Food and Drug Administration (FDA) approved daily oral TDF/FTC (tenofovir disoproxil fumarate/emtricitabine, *Truvada*<sup>®</sup>) for PrEP in 2012<sup>3</sup> and the US Centers for Disease Control and Prevention (CDC) released clinical guidelines on its use in 2014.<sup>4</sup> It is reported that there are now at least 125,000 people on PrEP in the US, the majority of whom are gay men.<sup>5</sup>

Many countries outside Europe – including Australia, Brazil, Canada, Kenya, Peru, South Africa and Thailand – are in the process of approving and/or introducing PrEP into HIV prevention programming.

The European region, however, has been surprisingly slow to respond to PrEP. Four years after the FDA ruling, in July 2016, the European Medicines Agency (EMA) gave a positive opinion on the use of *Truvada*<sup>®</sup> “for pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually-acquired human immunodeficiency virus type 1 (HIV-1) infection in adults at high risk.” It added that “Truvada is the first medicine recommended to reduce the risk of HIV infection in the EU. It is to be used as part of an overall HIV infection prevention strategy, notably including condom use, that can not only prevent HIV infection but also other sexually transmitted infections.” EMA notes that its recommendation is based on the evidence dossier submitted by *Truvada*<sup>®</sup> manufacturers Gilead Sciences, drawn from only the iPrEx and Partners PrEP studies and not the published results from PROUD and IPERGAY (see below).

On 22 August 2016, the European Commission officially granted marketing authorisation for once- daily *Truvada*<sup>®</sup> in combination with safer-sex practices to reduce the risk of sexually acquired HIV-1 infection among uninfected adults at high risk.<sup>6</sup> The marketing authorisation allows for the marketing of *Truvada*<sup>®</sup> for PrEP in all 28 countries of the European Union, subject to national regulatory authority approval of required pharmacovigilance materials in each country.

As of April 2017, the only countries in which PrEP is currently available within the national health system are Norway and France. In France, this is currently enabled under a temporary authorisation (*Recommandation Temporaire d’Utilisation* – RTU) for off-label use of *Truvada*<sup>®</sup> based on unmet therapeutic need and a favourable risk/benefit ratio. In Switzerland, *Truvada*<sup>®</sup> is recommended by the Swiss Commission for Sexual Health. PrEP can be prescribed off-label but it is not reimbursed. In Sweden, the Swedish Medical Products Agency gave approval for PrEP in August 2016 but PrEP is not yet available. In the UK, PrEP is due to be made freely available in Scotland in summer 2017 but in Wales and England this will only be through clinical studies. No other European countries have as yet initiated steps to introduce PrEP.

<sup>2</sup> <http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/>

<sup>3</sup> <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm312210.htm>

<sup>4</sup> <http://www.cdc.gov/vitalsigns/hivPrEP/index.html>

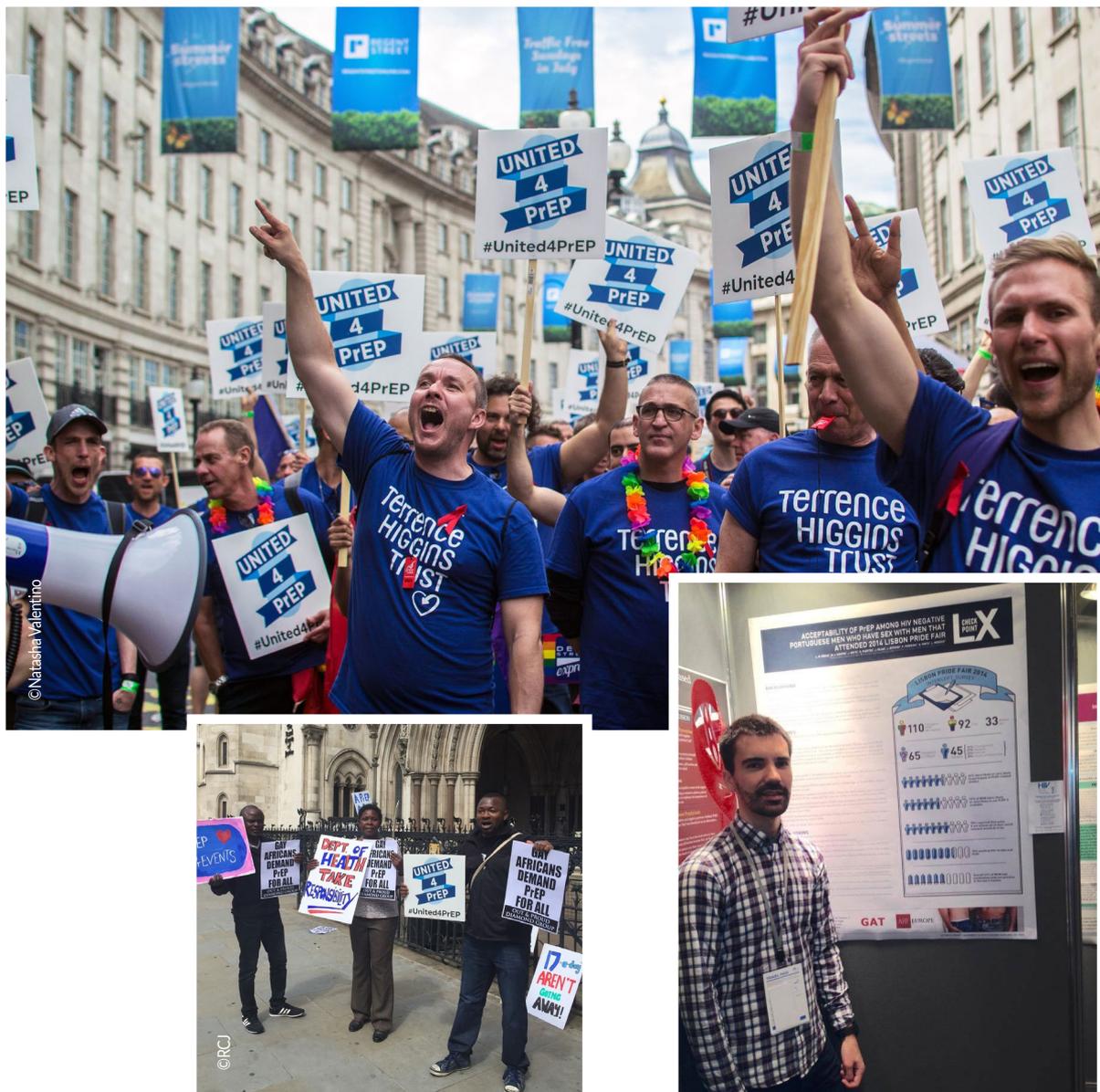
<sup>5</sup> Rawlings K et al. (McCallister S presenting) *FTC/TDF (Truvada) for HIV pre-exposure prophylaxis (PrEP) utilization in the United States: 2013-2015*. 21st International AIDS Conference, Durban, abstract TUAX0105LB, 2016.

<sup>6</sup> <http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-newsArticle&ID=2196665>

## About this report

This report seeks to provide a snapshot of PrEP access and uptake across the European region based on what HIV organisations and community networks have witnessed so far. PEI retrieved this information about PrEP access by putting out a call to all members of EATG, a network with reach across all 53 countries in the European region.<sup>7</sup>

The report begins with a review of the clinical trials and demonstration projects conducted in Europe to date, and information about those that are planned. It then walks through the guidelines on PrEP that have been published so far for the region as a whole and in individual countries and the process by which PrEP is approved and introduced at the national level. The second half of the report presents the information we have so far on PrEP uptake and use across the European region. This is based on anonymous input received so far from individuals based in 30 countries, including 24 of the 28 member states of the European Union (including the UK).



<sup>7</sup><http://www.euro.who.int/en/countries>

## Clinical trials of PrEP conducted in Europe

### IPERGAY, France ([www.ipergay.fr](http://www.ipergay.fr))

The first efficacy trial of PrEP to take place in Europe was IPERGAY, sponsored by the French National Institute for Health and Medical Research-French National Agency for Research on AIDS and Viral Hepatitis (Inserm-ANRS).<sup>8</sup> The placebo-controlled trial recruited 400 men who have sex with men (MSM) in six trial sites across France and a sister site in Montréal, Canada, and looked at intermittent use of PrEP. The regimen consisted of a double dose of *Truvada*® 2-24 hours prior to sexual intercourse, followed by a dose 24 hours after intercourse and another 48 hours after intercourse. Results showed a reduction in HIV risk by 86%. Annual incidence in the placebo arm was 6.6% and in the PrEP arm 0.91%, meaning that the number needed to treat (NNT) in order to avert one HIV infection was 18. After an interim analysis showed PrEP was protective against HIV in October 2014, randomisation was stopped and all trial participants offered intermittent PrEP. Just one more infection occurred in the open-label phase of the trial, generating an overall effectiveness during the trial of PrEP versus placebo of 97%.

### PROUD, UK ([www.proud.mrc.ac.uk](http://www.proud.mrc.ac.uk))

The PROUD pilot study<sup>9</sup> began in October 2012 and enrolled 544 MSM across six cities in England. Sponsored by the UK's Medical Research Council, its primary aim was to assess whether, if participants knew they were taking PrEP, their risk behaviour would change. It aimed to assess a number of other factors including who takes up the offer of PrEP and whether adherence behaviour changes over time. Similar to IPERGAY, randomisation stopped in October 2014 and all participants in the deferred arm were offered PrEP after an interim analysis showed an 86% reduction in HIV risk. Annual incidence in the deferred arm was 9.0% and in the immediate arm 1.2%, yielding a number needed to treat of 13. The trial was planned to continue till the end of 2016, though some clinics had to exit participants early due to issues with human resource funding. The continuing delay by NHS England in starting IMPACT, their large planned implementation study, has left options for PROUD participants uncertain in the short term.<sup>10</sup> Participants were informed at the end of the study in May 2017 that many of them, depending on the drug stocks remaining at their clinics, would have to rely on buying PrEP online until IMPACT starts.



<sup>8</sup> <http://www.nejm.org/doi/full/10.1056/NEJMoa1506273#t=article>

<sup>9</sup> [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(15\)00056-2/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)00056-2/abstract)

<sup>10</sup> <https://www.theguardian.com/society/2016/may/31/nhs-refusal-fund-hiv-aids-prevention-treatment-shameful-say-charities>

## Demonstration projects in Europe to date

Demonstration studies are designed to show how PrEP might be delivered in a national context and in many countries are the first step to providing PrEP access under medical supervision.

### **AMPrEP, the Netherlands ([www.ggd.amsterdam.nl/infectieziekten/soa-hiv-sense/prep/](http://www.ggd.amsterdam.nl/infectieziekten/soa-hiv-sense/prep/))**

The AMPrEP study is a one-centre trial in Amsterdam. Within 24 hours of recruitment, the demonstration project had received 350 applications, just shy of its 370 target. Participants are given the choice to select daily or intermittent PrEP and the results on uptake, acceptability and use are expected in 2018. AMPrEP is part of a wider HIV prevention initiative in Amsterdam known as the H-TEAM, a joint venture with the Amsterdam Institute of Global Health and Development (AIGHD), Stichting HIV Monitoring (SHM), Soa Aids Nederland, Public Health Service Amsterdam (GGD Amsterdam), the patient association Hiv Vereniging Nederland, the National Institute for Public Health and the Environment (RIVM), and general practitioners and hospitals in Amsterdam.

### **Be-PrEP-ared, Belgium ([www.be-prep-ared.be](http://www.be-prep-ared.be))**

Similar to AMPrEP, the Be-PrEP-ared study in Antwerp is a feasibility study of PrEP as a potential addition to the existing HIV-prevention strategy in Belgium, conducted by the Institute of Tropical Medicine. In this study, 200 MSM will be followed up for 18 months, using PrEP daily or intermittently to reduce their HIV risk. The trial began in September 2015 and will conclude in 2018.

### **DISCOVER**

DISCOVER, a large non-inferiority study is currently underway in North America and Europe, of the new alternative to *Truvada*<sup>®</sup>, *Descovy*<sup>®</sup>.<sup>11</sup> This drug substitutes the old formulation of tenofovir, tenofovir disoproxil fumarate (TDF) with a new one, tenofovir alafenamide (TAF), both in combination with emtricitabine. TAF is already licensed for HIV treatment. It reaches higher intracellular levels and lower plasma levels and thus requires a lower dose and produces fewer kidney- and bone-related side-effects. Its efficacy as PrEP in humans is unknown as yet, as we only have results from a monkey-model study. So far, 35 centres in nine European countries have registered interest in joining the study: Austria, Denmark, France, Germany, Ireland, Italy, the Netherlands, Spain and the UK.

### **Other demonstration studies**

In Spain, a proposal for a 400-participant demonstration project of *Truvada*<sup>®</sup> in MSM and trans women in community HIV clinics in Barcelona and Madrid was proposed. After consideration, the Ministry of Health rejected this idea and has instead proposed a demonstration project restricted to people who approach hospital-based HIV clinics and obtain PrEP from hospital pharmacies, i.e. in the same way that PEP (post-exposure prophylaxis) is currently available. The proposers of the original study have contested this idea as very restrictive in terms of who is likely to present themselves for PrEP. At present negotiations are ongoing.

In Athens, Greece, discussions on a small 200-participant pilot demonstration project are ongoing. A number of other countries in Europe, including Denmark, Ireland, Israel, Luxembourg, Portugal and Sweden are believed to be currently in the process of planning their own PrEP demonstration projects in key cities. In the east of the region, Azerbaijan, Georgia and Ukraine are also exploring PrEP projects.

<sup>11</sup> <https://clinicaltrials.gov/ct2/show/NCT02842086?term=NCT02842086&rank=1>

## European-wide guidelines on PrEP

The European AIDS Clinical Society (EACS) published its first guidelines on PrEP in October 2015 as part of its updated 2015 Treatment Guidelines, following updated WHO guidance a few weeks prior (version 8.0).<sup>12</sup> The EACS guidelines state that PrEP can be used by adults at high risk of acquiring HIV infection, with PrEP recommended for HIV-negative MSM and transgender individuals who are inconsistent in their use of condoms with casual partners or with HIV-positive partners who are not on treatment. A recent sexually transmitted infection (STI) or use of PEP are listed as possible markers for increased risk for HIV acquisition. The guidelines also state that PrEP may be used by heterosexual women and men who are inconsistent in their use of condoms or who are likely to have HIV-positive partners who are not on treatment. EACS recommends intermittent PrEP for use only by MSM and daily PrEP for use by all others at substantial risk.

## National-level guidelines and recommendations

### France

In France, PrEP is currently recommended under an emergency measure (*Recommandation Temporaire d'Utilisation – RTU*) for everyone over 18 years of age who does not systematically use a condom during sex and who is at high risk for contracting HIV, in particular:

- Gay men and trans individuals who have sex with men (if certain criteria apply: PEP or STI during the past 12 months or 2 instances of anal sex without a condom during the past 6 months).

Other populations that are vulnerable to HIV, such as sex workers, migrants from high-prevalence regions (sub-Saharan Africa, Guyana, etc.), people who inject drugs, and people with multiple sexual partners will be considered for PrEP on a case-by-case basis. It is the physician's responsibility to assess this risk with the individuals concerned, to check for any potential contraindications, and, in the end, to decide whether or not to prescribe PrEP.

### Norway

On 20 November 2016, Norway became the second European country to approve PrEP, and the first to make it completely free on demand by people seeking it who fell within risk criteria as defined by the EACS guidelines (see above). As a non-EU nation, PrEP is licensed in Norway by the Norwegian Medicines Agency, which evaluates and decides whether a medicine should be reimbursed by the National Insurance Scheme.

### UK

In the UK, the British HIV Association (BHIVA) and the British Association for Sexual Health and HIV (BASHH) first published a position statement on PrEP in January 2012, which was most recently updated in April 2016. BASHH and BHIVA strongly recommend that PrEP be made available within a comprehensive HIV prevention package to:

- MSM and trans women who are engaging in condomless anal sex.
- Heterosexual and same-sex, HIV-negative partners who are in relationships with HIV-positive partners whose viral replication is not suppressed.
- Other heterosexuals considered to be at high risk.

<sup>12</sup> [http://www.eacsociety.org/files/guidelines\\_8\\_0-english\\_web.pdf](http://www.eacsociety.org/files/guidelines_8_0-english_web.pdf) - PrEP guidance is on page 15.

## Denmark

In 2015, the Danish Society for Infectious Diseases stated: “PrEP should be considered for MSM who are not HIV-infected and who regularly have condomless anal intercourse with different partners. Repeated occurrence of STIs can be used for identifying the persons who meet these conditions”. However, it did not recommend PrEP for heterosexual individuals: “Currently as far as we know HIV transmission among heterosexuals in Denmark has not reached a degree that justifies the use of PrEP in such situations.” The Danish guidelines define PrEP as “a daily dose (1 tablet *Truvada*) or ‘on demand’ with a double dose of 2-24 hours prior to sexual intercourse, followed by a dose of 24 and 48 hours after. A combination of tenofovir and lamivudine may be used instead of *Truvada*”.<sup>13</sup>

## Spain

The GeSIDA group of the Spanish Society of Infectious Diseases and Clinical Microbiology released Spanish Guidelines on PrEP in June 2016.<sup>14</sup> They recommend that PrEP should be offered to MSM and trans women who have had condomless sex in the last six months AND

- Have had more than two partners OR;
- An STI diagnosis OR;
- Have sought PEP OR;
- Have had ‘chemsex’.

They also recommend that PrEP may be considered for people who are not MSM or trans women where the person:

- Is in a serodiscordant relationship with an HIV-positive person with an unsuppressed viral load.
- Injects drugs and has shared equipment.
- Has had transactional sex for food or shelter.
- Is otherwise socially vulnerable and at high risk of HIV.

## Sweden

In February 2016, the Reference Group for Antiviral Therapy (RAV) published new treatment guidelines for people living with HIV recommending PrEP for “people most at risk”<sup>15</sup>, clarified as follows: “The risk of infection to people whose partners are taking ARV [antiretroviral] treatment is considered minimal. The group where HIV transmission in Sweden is the most common is MSM. In this group, however, the number of newly diagnosed cases has decreased in recent years, so only a limited number of transmissions could be prevented with PrEP. PrEP should be seen as a protection option for individuals with high sexual risk-taking. There is continuing infection risk in foreign destinations where sexual contacts are made. These may be individuals who would benefit from PrEP”.<sup>16</sup> The Swedish Medical Products Agency gave approval for *Truvada*<sup>®</sup> to be prescribed as PrEP in August 2016. However due to the high costs related to PrEP delivery, it is not yet available on the national health system.

## Switzerland

The Swiss guidelines on PrEP were published on 25 January 2016 by the Swiss Federal Commission for Sexual Health (FCSH)<sup>17</sup>, recommending PrEP “only for limited periods and only for a small group of persons at substantial risk of acquiring HIV, for whom consistent condom use is not a viable option, and where regular prophylactic use of antiretroviral drugs will enable them to engage in sexual activity without fear”. According to the guidelines, high risk may be indicated by recently acquired infections such as syphilis, use of so-called ‘chemsex’ drugs, or repeated use of PEP.

<sup>13</sup> [http://www.infmed.dk/guidelines#pre\\_exposure\\_profylakse\\_mod\\_hiv\\_2015.pdf](http://www.infmed.dk/guidelines#pre_exposure_profylakse_mod_hiv_2015.pdf)

<sup>14</sup> [http://www.gesida-seimc.org/contenidos/guiasclinicas/2016/gesida-guiasclinicas-2016-profilaxis\\_pre-exposicionVIH.pdf](http://www.gesida-seimc.org/contenidos/guiasclinicas/2016/gesida-guiasclinicas-2016-profilaxis_pre-exposicionVIH.pdf)

<sup>15</sup> [http://www.sls.se/Global/RAV/Dokument/RAV\\_HIV\\_2016\\_160410.pdf](http://www.sls.se/Global/RAV/Dokument/RAV_HIV_2016_160410.pdf)

<sup>16</sup> Translated by google.

<sup>17</sup> [http://www.bag.admin.ch/hiv\\_aids/05464/12494/12821/index.html?lang=en](http://www.bag.admin.ch/hiv_aids/05464/12494/12821/index.html?lang=en)

The guidelines specify that PrEP should be prescribed and monitored by physicians with experience both in the provision of sexual health advice and in the use of antiretroviral drugs. In Switzerland, HIV drugs are not approved for prophylactic use: “Physicians who prescribe oral chemoprophylaxis for HIV prevention do so on an off-label basis and are thus liable for any adverse effect that may occur. The drug costs are not reimbursable under compulsory health insurance.”

The Commission guidelines are unusual in that they include reflections on cost-effectiveness, citing the UK study<sup>18</sup> on this published in 2015: “The FCSH takes the view that, over the long term, financial resources for HIV prevention are best deployed if the number of infectious individuals continues to be effectively reduced by consistent compliance with the “safer sex” rules, by early diagnosis and treatment, and by timely interruption of chains of transmission in the early stages of HIV infection. Prescription of PrEP may well be indicated in certain cases”.

## European surveys of PrEP use

Two surveys conducted on PrEP knowledge and use in Europe in 2016 reported rather different findings. In April 2016, the European Centre for Disease Prevention and Control (ECDC) collaborated with the Hornet gay social network on a rapid survey of men who have sex with men in Europe.<sup>19</sup> Over three days, 8543 people responded to the survey. Of these, 26% were from France, 22% from the UK and 10% from Russia, reflecting the reach of Hornet in these countries. Among the 8048 respondents who did not report being HIV positive, 793 (10%) reported that they were currently taking PrEP. The fact that far more French respondents reported obtaining PrEP from their physician and far fewer from internet sources reflects that country’s provision of PrEP through its health service.

Another survey of knowledge and use of PrEP in Europe released its preliminary results on World AIDS Day (1 December) 2016. The Flash! PrEP in Europe survey had 15,880 respondents.<sup>20</sup> Seventy per cent were from Germany, where the gay social network site Gayromeo promoted the survey intensively. It found high, though varying, levels of knowledge about PrEP among respondents. For instance, 62% of gay men outside Germany had correct knowledge of PrEP but only 30% of German men and 27% of female respondents. Five per cent of gay men with knowledge of PrEP (4% in Germany) had used PrEP informally, i.e. obtaining it online or from friends, but two-thirds had no medical support or monitoring for their PrEP use. Most people thought it should be offered through public health systems and a majority thought it should be provided free of charge or at least partly covered by health insurance.

<sup>18</sup> Cambiano V, Miners A, Dunn D T, McCormack S, Gill O N, Nardone A, et al. Is pre-exposure prophylaxis for HIV prevention cost-effective in men who have sex with men who engage in condomless sex in the UK? *Sex Transm Infect* 2015; 91: O1.

<sup>19</sup> See <http://ecdc.europa.eu/en/publications/Publications/pre-exposure-prophylaxis-hiv-prevention-europe.pdf>

<sup>20</sup> See <http://www.aides.org/FlashPrEPinEurope> and [http://www.aides.org/sites/default/files/Aides/bloc\\_telechargement/ResultPrepGB\\_vf.pdf](http://www.aides.org/sites/default/files/Aides/bloc_telechargement/ResultPrepGB_vf.pdf)

## PrEP approval processes in Europe

The regulation of medicines in Europe is ultimately a national responsibility. However, in 1995, to streamline and harmonise this process, the EU established a European Medicines Agency (EMA) with the authority to evaluate medicines for use across the European Union as a whole.

In January 2016, Gilead Sciences announced that it had submitted an application to the EMA for approval of *Truvada*<sup>®</sup> as PrEP. The EMA announced on 22 July 2016 that its Committee for Medicinal Products for Human Use (CHMP) had adopted a positive opinion on the use of *Truvada*<sup>®</sup> for PrEP.

Now that marketing authorisation has been granted by the European Commission, decisions about price and reimbursement will take place at the level of each Member State considering the potential role and use of the medicine in the context of the national health system of that country. The EMA's positive opinion on PrEP will most strongly influence the availability of PrEP in Europe in the countries where EMA approval is a prerequisite for approval by that national regulatory authority. However, as regulators, the EMA decision is a purely medical recommendation and it has no opinion on reimbursement. It is the question of how the diverse healthcare systems of Europe will provide and pay for PrEP that now poses the biggest barrier to access.

With tenofovir disoproxil, which in its fumarate salt (TDF) forms one of the drugs in *Truvada*<sup>®</sup> (the other being emtricitabine or FTC) coming off patent in many countries in July 2017, generic manufacturers are seeking marketing authorisation for their equivalent tenofovir products. To date, the EMA's CHMP has recommended the granting of a marketing authorisation of *Truvada*<sup>®</sup> equivalents as a treatment for HIV to two generic manufacturers: Zentiva<sup>21</sup> and Krka d.d. (based in Slovenia).

With PrEP, the situation is rather different. Because the EMA authorisation was only given to the *Truvada*<sup>®</sup> fixed-dose combination pill, whether the patent can be extended on *Truvada*<sup>®</sup> is crucial to whether generic equivalents can be used as PrEP. Gilead Sciences, which owns the patent for *Truvada*<sup>®</sup>, may have patent rights until as late as 2021. While this patent exists, it prevents other companies from making and selling much cheaper single pill versions of tenofovir/emtricitabine (the drugs that are combined to make single pill *Truvada*<sup>®</sup>). Four generic manufacturers of these cheaper pills are challenging this extended patent in the Court of Justice in the EU, but if Gilead does not withdraw, it could take many months (or longer) to get a ruling. In the meantime Gilead has a monopoly, and is able to charge unaffordably high prices.

At present, the lower-income countries of central and eastern Europe are showing very little interest in PrEP, despite infections in MSM rising particularly fast in this area. The Bulgarian Ministry of Health has stated already that they have ruled out PrEP provision: "The Ministry of Health and a number of HIV specialists here are absolutely against the provision of PrEP to high-at-risk populations and this is out of the question now," comments one of our respondents.

<sup>21</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2016/09/news\\_detail\\_002599.jsp&mid=WC0b01ac058004d5c1](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/09/news_detail_002599.jsp&mid=WC0b01ac058004d5c1)

## PrEP in England

A subcommittee of the HIV Clinical Reference Group for NHS England was set up to make recommendations for the provision of PrEP in England in September 2014. Its recommendations, which were ultimately not adopted, were that PrEP should be made available for persons who are:

- ▶ MSM and trans women who are currently HIV negative and who are clinically assessed to be at high risk of HIV acquisition through fulfilling the following criteria:
  - Have a documented confirmed HIV-negative test result during an earlier episode of care in the preceding year (i.e. 42-365 days ago); and
  - Report condomless intercourse in the previous 3 months and this is documented in the clinical notes; and
  - Affirm their likelihood of repeated condomless intercourse in the next 3 months and this is documented in the clinical notes.

OR

- ▶ The HIV-negative partner (confirmed by a current documented HIV-negative test result) of a diagnosed person with HIV who is not known to be virally suppressed and with whom condomless intercourse is anticipated and so is clinically assessed and considered to be at high risk of HIV acquisition. PrEP should be recommended where the treating clinician recommends and monitors treatment as part of an active risk reduction intervention including health education, safer sex promotion, and exploration of treatment as prevention for the HIV-positive partner;

OR

- ▶ HIV-negative heterosexual men and women clinically assessed and considered to be at similar high risk of HIV acquisition as those with a serodiscordant partner. PrEP should be recommended where the treating clinician recommends and monitors treatment as part of an active risk reduction intervention including health education and safer sex promotion.

In 2016, however, NHS England announced that it would not be taking this recommendation forward due to lack of clarity about who would be responsible for a PrEP programme. Following a legal challenge by the National AIDS Trust, the UK Court of Appeal ruled that NHS England has the power, although not the obligation, to fund PrEP and should plan how to provide it. As a result, NHS England is funding a large-scale PrEP 'trial' across England, to start in mid-2017.

The eligibility criteria will likely include:

- \* cis- and transgender men who have sex with men, and transgender women who are HIV negative, report sex without condoms in the past 3 months, and consider that they will do so again in the next 3 months;
- \* the HIV-negative partner of an HIV-positive person when the positive partner is not known to be virally suppressed and sex without condoms is anticipated;
- \* other populations who are clinically assessed and considered to be at similar high risk of HIV acquisition.

In April 2017, the Scottish Medicines Consortium (SMC) announced that daily or intermittent PrEP can be prescribed by the NHS in Scotland. The All Wales Medicines Strategy Group advised that the NHS should not provide PrEP in Wales. In response, the Wales Health Minister Vaughan Gethin announced a study to learn how best to provide PrEP to reduce HIV transmission in Wales and answer some of the questions raised by the Strategy Group around incidence rates.

## Prescribing of *Truvada*<sup>®</sup> off-label

Research by PEI has uncovered anecdotal evidence that HIV doctors are currently prescribing *Truvada*<sup>®</sup> off-label to HIV-negative individuals in at least ten countries in Europe, of which most, but not all, are within the EU. In most of these situations, these are private clients paying the full cost of the drug. It is not clear if these PrEP users are receiving medical supervision along with the full PrEP package of services including HIV and STI screening and kidney function tests or just receiving a prescription.

*AUSTRIA: "According to the doctors there is a demand for PrEP. One of the major problems however is the price. The only way to get the PrEP off-label is that you pay the full price that it costs in Austria. Getting PrEP over the internet is not allowed in Austria. Therefore, it is also hard for the doctors to do the official check-ups that are reimbursed by the insurance. So actually, if you want to take PrEP off-label you have to pay for the medicine and for the check-ups privately."*

*BELGIUM: "What I heard from these doctors is that they prescribe Truvada and ask their patients to engage in follow up appointments to check renal functions, STI screening & drug levels. One STI-clinic testified that there are some 5 to 10 patients per doctor in such centres prescribing on demand to their patients. These patients are MSM only. Since PrEP is not yet officially recognised as such nor reimbursed, patients have to pay the full amount for their prescription (close to €500/month)."*

*CROATIA: "I asked the clinicians if they have ever done so, and they have said no. Even if they did it wouldn't be covered by insurance, the price is very high, and a monthly dose is close to the average monthly income."*

*IRELAND: "PrEP is only available to be dispensed from one pharmacy, based in the Sexual Health clinic (GUIDE) at St James' Hospital and comes at the full price (around €400 for a month). I would also imagine there would be extra cost involved for liver [and] renal function tests and regular HIV tests if in the private system."*

In several countries, such as Germany, Denmark and Italy, it was reported that doctors are unable or unwilling to prescribe off-label due to fear of prosecution.

*ITALY: "Some clinicians are prescribing it off-label in some cases. Formally, it should be against the rules ...clinicians prescribing Truvada as PrEP could be asked to explain what he or she did to medical authorities. In Italy, there is a special registry for off-label use of medicines and Truvada for prevention is not included in it."*

*CZECH REPUBLIC: In the Czech Republic, HIV doctors are apparently unwilling to prescribe because they do not support the concept of PrEP. Some people noted that an EMA ruling in favour of Truvada as PrEP may make an important difference for HIV physicians in this regard: "There is no legal barrier to prescribe Truvada off-label. Truvada can be prescribed off-label outside the health insurance system, i.e. if paid in full by the user (price tag of approx. 550 EUR/month). However, HIV centre doctors resist prescribing Truvada as PrEP as they object to the whole idea of PrEP and general practitioners do not have enough information and experience with PrEP. If prescribed off-label, the drug can still be dispensed only in selected pharmacies in the country that supply drugs to HIV centre patients."*

*CYPRUS: "Truvada is not available in the private pharmacies, so only governmental doctors that work in the HIV field can prescribe Truvada and only to people living with HIV or as PEP."*

*MACEDONIA: "Once there is an official prevention indication by EMA for Truvada, it might become easier to convince a doctor to give a prescription, but it's not clear"*

## “DIY PrEP”: Informal PrEP use

Anecdotal evidence of informal PrEP use, whereby people access *Truvada*<sup>®</sup> outside public and private health systems, is growing across the region. Our research found that “Do-It-Yourself (DIY) PrEP” is taking place in at least 20 countries in the region, including in countries where doctors are not able or willing to prescribe. Stories are also emerging of a black market for *Truvada*<sup>®</sup>, whereby people in financial need sell their pills. The street value of one pill of *Truvada*<sup>®</sup> has been heard to be €25.

It should be noted that not all informal PrEP users are doing so without medical supervision. Some users are seeking medical advice and services, but accessing PrEP outside of the formal system.

People in Europe are reportedly taking DIY PrEP in the following creative ways:

### 1. “Clinic-hopping” or PEP as PrEP

In some settings, it is possible to obtain *Truvada*<sup>®</sup> by presenting at clinics for PEP, then discarding the remaining regimen. Clinic-hopping is not possible in countries like Germany where PEP is prescribed through a physician. Clinics that notice increased demand may decide to tighten access to PEP, which has worrying implications. Community-based testing sites and networks in Austria, Greece and Spain report hearing about this:

*SPAIN: “Last week on the national TV the news mentioned that some doctors have spotted that some of the people who went to the hospital for PEP came on a regular basis and probably they use the Truvada for PrEP.”*

*GREECE: “What we unofficially know, there are some people who do what is called “clinic hopping”, namely they “continuously” get PEP from the Special Infections Units of the Public Hospitals in Athens and they use it as PrEP.”*

### 2. Pill-sharing

Some people are accessing PrEP through their HIV-positive friends, who either share the *Truvada*<sup>®</sup> pills that are no longer needed by them for treatment, or by going back to clinics for more, stating they have lost the prescription or the bottle. This has been heard of in Austria, Belgium, Bulgaria, Croatia, Ireland and Sweden:

*BELGIUM: “We heard marginal stories of people ‘having lost their prescription’ and asking for a new one from their physician, but this was just one story.”*

*CROATIA: “There are anecdotal stories about some people living with HIV giving their Truvada to negative friends and asking for an extra bottle saying they have lost it. It is possible this is happening, but at a very small scale, as it would be noticed by the clinic if it were on larger scale. We only have one clinic and pharmacy with HIV drugs in Croatia.”*

### 3. Smuggling

People are also asking friends who live abroad to bring *Truvada*<sup>®</sup> into the country for them or bringing it into the country from abroad themselves. This was reported in Austria, Belgium, Cyprus, Germany and Norway.

*CYPRUS: “From what we learn from unofficial sources they are a few people getting PrEP from abroad.”*

*AUSTRIA: “We actually just had our first “public” presentation of a doctor in the community about PrEP – I have heard that people are asking friends to bring Truvada into the country.”*

#### 4. Ordering generic PrEP online

As described on the I Want PrEP Now website, it is possible for people to purchase a generic version of *Truvada*<sup>®</sup> from online pharmacies. The UK HIV information website i-Base recommends [www.aids-drugs-online.com](http://www.aids-drugs-online.com), [www.alldaychemist.com](http://www.alldaychemist.com) and [www.unitedpharmacies.com](http://www.unitedpharmacies.com).<sup>22</sup>

Most countries in Europe block these imports at customs. Therefore, customers are using parcel forwarding options based in countries that do allow generic drug importation (notably the UK, which permits three months' supply of medicine for personal use). Some clinics are offering drug-level testing in recognition of the fact that people need to know they are taking a quality-assured drug. This method of accessing PrEP appears to be increasingly popular in Denmark, Germany, Ireland and Portugal, and was also reported further east in Greece, Macedonia and Bulgaria.

*DENMARK: "We hear of people using Truvada informally. They buy it from some website in Malaysia or import it through England, Thailand or Australia."*

*GERMANY: "The only legal way to do this is to travel to the UK and bring the pills with you in your own luggage. That's quite a barrier, so people are asking friends in the UK to receive the order and send on privately, or using parcel forward delivery services that use a UK PO box then forward the parcel to Germany from there. To ensure it gets through customs, the parcel is declared as having £30 value and as containing dietary supplements."*

*IRELAND: "It is possible for people to order generic Truvada online to a UK address which is then redirected. Anecdotally, this passes through customs and VAT is applied before delivery with no further issues."*

*PORTUGAL: "To overcome customs, people are asking friends from UK to receive the online order and resend it to Portugal by private post mail."*

*GREECE: "ARVs in Greece can only be distributed through pharmacies in public hospitals. That means that any attempt to buy them (generic or not) online would be blocked in the customs. The only way someone could bring in generic Truvada would be to use someone in a country where importing is legal and then post it to them."*



<sup>22</sup> See <http://i-base.info/qa/10734>

MACEDONIA: “In Macedonia one could order by internet or by post medicines for personal use and it can well be generic TDF/FTC. The person needs to obtain an importation licence from the Medicines Agency by submitting a request stating the purpose, the exact product, the quantity etc. plus a prescription or an opinion by a specialist. The procedure is relatively quick (1-2 days) and there is no fee. With the issued license, the person can go to the Customs Office and obtain the product. As far as I know, it is not possible to receive it at home, but you need to go to the Customs where they will have retained the package.”

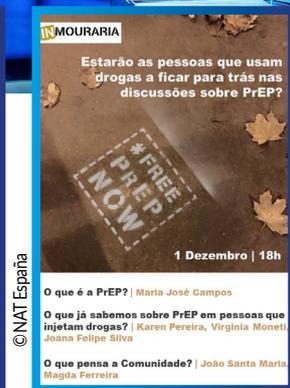
BULGARIA: “There is certain resistance about generics as many of them are produced in countries like India which is an argument about their lower quality or risk involved. Nevertheless, if someone decides to buy online or bring through the border generics for personal use it is ok and I believe some people do it.”

### 5. Parties

Gay party organisers are starting to include Truvada® in their “party packages” that contain Truvada® alongside condoms. This has been reported in Belgium and Germany.

BELGIUM: “We did hear stories of people selling Truvada on a party bus coming from Paris going to Brussels to a gay party.”

GERMANY: “I’ve heard of sex party packages where you pay an administration fee and that includes catering, condoms, recreational drugs and some pills of Truvada.”



## Conclusion and recommendations

PrEP has arrived in Europe, but in too many cases it is being taken without medical supervision and on an ad-hoc basis that could undermine its proven effectiveness. The official authorities are playing catch up, and failing in their duty to protect public health.

The word has gone out to gay men – an internationally mobile community – that *Truvada*<sup>®</sup> is highly effective at preventing HIV and they are taking it to reduce their risk of infection. Those with sufficient disposable income and access to a sympathetic physician are able to access *Truvada*<sup>®</sup> by paying the cost price of around 500-850 euros/month for a 30-pill bottle. Those without such resources are accessing it from places where they know *Truvada*<sup>®</sup> is readily available, but are often having to lie or deceive to obtain it. It is also being offered to them by friends, party organisers and others looking to make money as a handful of pills that is unlikely to confer protection. To address this, PrEP activists are promoting safer and cheaper ways to access PrEP by promoting importation of generic PrEP. Clinics, for their part, are offering to monitor *Truvada*<sup>®</sup> levels with no questions asked as to how the clients source their pills.

Without official PrEP approval and roll-out within health care and community settings, many people will end up taking a few pills of *Truvada*<sup>®</sup> without knowing their HIV status, STI status, renal health and risk factors. Many of them may take PrEP needlessly, or worse, within an acute HIV infection phase. These people may also be vulnerable to being sold counterfeit versions of *Truvada*<sup>®</sup> as a black market emerges. Without clear information about how PrEP works, people from communities most at risk will be unable to use and adhere to PrEP safely and effectively.

With the European Commission granting marketing authorisation, it is now imperative that European member states begin the process of introducing PrEP into their HIV prevention programmes, drawing on guidelines already developed by the European AIDS Clinical Society and their HIV associations. In addition, accurate information about PrEP needs to be made available urgently to communities of people at risk of HIV to ensure they can access and adhere to PrEP effectively.



**We call on European governments to:**

- Make PrEP available to populations at high risk of HIV as a matter of urgency.
- Embed PrEP within improved and expanded access to HIV prevention tools and strategies, particularly for key affected populations.
- Make public information about PrEP widely available, especially among key populations, so people can judge their HIV risk and their need of PrEP, of its dosing, benefits and possible risks.
- Continue their role as key funders of HIV prevention research programmes, including vaccines and microbicides.

**We call on Gilead Sciences to:**

- Surrender its Supplementary Protection Certificate for the *Truvada*<sup>®</sup> fixed-dose combination pill, in order to allow generic equivalents of *Truvada*<sup>®</sup> to be sold as PrEP from 2017.
- Be open about its intentions to market PrEP in Europe once tenofovir disoproxil comes off patent in 2017.
- Be open about its research programme and marketing strategy for TAF (tenofovir alafenamide) as PrEP and its *Truvada*<sup>®</sup> equivalent, *Descovy*<sup>®</sup>, and work with the community and researchers to ensure that appropriate trials are conducted ethically and safely.
- Ensure all trial participants in demonstration projects for *Truvada*<sup>®</sup> have access to PrEP post-trial.
- Clarify the question of whether intermittent PrEP works as well as daily PrEP for women or for men whose exposure to HIV is solely penile/urethral.

**We call on generic manufacturers of antiretrovirals to:**

- Seek marketing authorisation in Europe for the use of generic versions of *Truvada*<sup>®</sup> as PrEP and not just as treatment.
- Address the supply issues that the demand for online PrEP has at times created.

**We call on European health authorities and HIV medical associations to:**

- Collaborate closely with key affected communities to develop detailed guidelines for PrEP usage and implementation drawing from the existing EACS guidelines already available.
- Collaborate closely with key affected populations to support the roll out of PrEP in community-based settings.
- Support continued PrEP implementation research among under-studied groups, including refugees and migrants, female sex workers, trans women and men, people who use drugs who are also at risk of HIV exposure through sex, people in prison settings, adolescents and other key affected populations.

**We call on the European Commission to:**

- Approve existing and forthcoming positive recommendations on generic versions of *Truvada*<sup>®</sup> from the European Medicines Agency (EMA) without delay.
- Continue to fund a co-ordinated programme of HIV prevention research, developed with the full involvement of affected communities to further understand which prevention programmes are most effective and acceptable in European contexts.
- Commission research and surveillance on the informal use of PrEP across the 28 member states of the European Union.
- Facilitate dialogue between governments, international organisations and the community on how to reduce rising HIV infection rates across the region.



# PrEP ACCESS IN EUROPE

PrEP in Europe Initiative (PEI)

