Rationale for resource

This resource is designed to support registered practitioners involved in the delivery of HIV pre-exposure prophylaxis in the NHS Scotland.

On the 10th April, 2017 Scotland became the first of the UK nations to approve the provision of PrEP by the NHS to prevent HIV.

The Scottish Medicines Consortium (SMC) announced that the drug Truvada® was deemed an effective treatment to prevent the transmission of HIV and will be made available through the NHS in Scotland.

The implementation date for this programme was July, 2017.

From 1st November 2017 Dr Reddy’s (Emtricitabine / Tenofovir Disoproxil Succinate) is the recommended supplier/preparation for PrEP.

Please note:
These educational resources continue to be updated as required to be support this programme but do not replace the clinical judgement of practitioners. Practitioners should refer to available guidance e.g. Scottish Medicines Consortium and BHIVA/BASHH position statement, https://www.scottishmedicines.org.uk/files/advice/emtricitabine_tenofovir_disoproxil_Truvada_FINAL_March_2017_for_website.pdf

Note: For the purposes of this resource HIV Pre-exposure prophylaxis will be known as HIV PrEP.
Key Messages

• HIV is a major public health challenge for Scotland with an annual average of 359 new cases in Scotland over the last 5 years
• Majority of HIV infections are sexually transmitted, with MSM* remaining the group at highest risk in Scotland
• PrEP is an effective HIV prevention intervention which uses anti-retroviral drugs to protect individuals at highest risk from acquiring HIV
• Studies conducted within the UK and international settings have found oral HIV PrEP to be effective in reducing sexual HIV transmission. These studies are mostly in MSM but there is also evidence of its effectiveness in heterosexual men and women
• The medication currently recommended for HIV PrEP is a fixed dose oral combination tablet. The combination tablet comprises of two antiretroviral drugs; Tenofovir and Emtricitabine.

TDS- Tenofovir disoproxil succinate
FTC-Emtricitabine

*The term MSM used here includes Men having sex with men and includes transgender men who have male sexual partners
Key Messages

• In April 2017, the Scottish Medicines Consortium accepted Truvada® for use as HIV PrEP in NHS Scotland in adults at high risk of HIV infection. From 1st November 2017 this was replaced by Dr Reddy’s (Tenofovir Disoproxil Succinate/Emtricitabine) as the recommended supplier in Scotland.

• From July 2017, NHS Scotland are offering HIV PrEP through specialist sexual health services to individuals who meet eligibility criteria as part of a wider targeted national prevention programme.

• HIV PrEP should not be seen as a replacement for condoms. Regular testing for HIV and other sexually transmitted infections (STIs) is essential.

• Effective and consistent provision of advice and clinical care (including monitoring) is essential for the successful implementation of the HIV PrEP programme in Scotland.
Role of registered practitioners

- Registered practitioners have a key role in supporting the introduction of the HIV PrEP programme in NHS Scotland

- This role includes the effective and consistent provision of advice and clinical care (including monitoring)
Aims of the resource

• To raise awareness of the current epidemiology of HIV in Scotland and the important role of PrEP in reducing the risk of HIV transmission

• To provide registered healthcare practitioners with an overview of the HIV PrEP programme to be delivered by specialist sexual health services in Scotland from July 2017, including eligibility

• To support registered practitioners involved in discussing and/or offering HIV PrEP to individuals in Scotland

• To highlight clinical aspects of the safe provision and monitoring of HIV PrEP medication
Learning outcomes
After completing the resource practitioners will be able to:

• Describe the current epidemiology of HIV in Scotland
• Understand the rationale and evidence base for a targeted HIV PrEP programme in Scotland and their role in delivering it
• Discuss with clients the benefits and clinical considerations associated with HIV PrEP
• Understand clinical aspects of the safe provision and monitoring of the HIV PrEP medication
• Identify sources of additional information

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• Why introduce HIV PrEP in Scotland?
• What is the evidence base for HIV PrEP?
• HIV PrEP implementation in NHS Scotland
  - Eligibility
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Why introduce HIV PrEP in Scotland?
HIV in Scotland

- Every year in Scotland new HIV diagnoses continue to be made with an average of 359 new diagnoses each year in the last 5 years
- The majority of infections are sexually transmitted
- Since 2011, MSM have accounted for 47% of all new HIV diagnoses compared to 38% for heterosexuals
- Since 2014, data indicate that a higher proportion of new diagnoses in MSM are as a result of recent (less than 6 months) infections (35%) compared with other risk groups (19%)
- MSM remain the group at highest risk of HIV in Scotland
Other/Unk = Other/Unknown
What is HIV PrEP?

- PrEP stands for ‘pre exposure prophylaxis’
- PrEP is considered an effective HIV prevention intervention
- PrEP is used by HIV negative people to prevent them from becoming HIV positive
- Anti-retroviral drugs are taken before potential exposure to HIV to reduce the risk of the virus establishing itself in the body
- PrEP forms one component of wider targeted HIV prevention for those at highest risk of HIV acquisition in Scotland
What is HIV PrEP? (contd.)

- HIV infection occurs over a short time. Even if sex lasted a few minutes, it takes about 30 minutes after sexual exposure for the virus to get through genital skin and enter the body.
- It then takes 2-3 days for the infection to become established in the body.
- For HIV PrEP to be most effective the medicine needs to be at protective levels throughout this period.
- HIV PrEP needs to be taken before sex and for several days afterwards.
What is HIV PrEP (contd.)?

- Medication currently recommended for HIV PrEP interventions is a single fixed dose oral combination tablet.
- HIV PrEP comprises of two antiretroviral drugs; Tenofovir and Emtricitabine.
HIV PrEP
part of a national intervention programme

• HIV PrEP is part of a wider targeted national prevention programme delivered by the NHS in sexual health services

• HIV PrEP should not be seen as a replacement for condoms, and regular testing for HIV and other STIs is crucial
**HIV PrEP- Licensing**

- Truvada® has been licensed in the UK and used in Scotland for a number of years as a treatment for people with HIV
- In 2016, the European Medicines Agency (EMA) licensed Truvada® for use as HIV PrEP
- This decision resulted in the manufacturer making a submission to the Scottish Medicines Consortium (SMC) using a New Product Assessment Form, which was accepted
- In April 2017, the Scottish Medicines Consortium accepted Truvada® for use as HIV PrEP in NHS Scotland in adults at high risk of HIV infection
- From 1st November 2017 this was replaced by Dr Reddy’s (Tenofovir Disoproxil Succinate/Emtricitabine) as the recommended supplier in Scotland

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Why is PrEP important?

Current interventions do not seem enough-
- Testing and treatment
- PEPSE*
- Behaviour change interventions
- Condoms

Comparison:

PEPSE = emergency contraception
What is the evidence for HIV PrEP?
HIV PrEP evidence
- PROUD Study

- The study was carried out in 13 sexual health clinics in England
- More than 500 MSM and/or transgender women were enrolled
- One group took daily PrEP as soon as they enrolled on the study (intervention group)
- One group took PrEP after a year (deferred group)

This study was an open-label design in which half of the 544 participants were randomly assigned to daily TDF/FTC in the first year and half were not.
HIV incidence was significantly lower in individuals assigned to immediate PrEP (1.2 cases per 100 person years) compared with the deferred group (9.0 cases per 100 person years). This corresponds to a proportionate reduction of 86% (90% CI 64-96). In October 2014, based on early evidence of effectiveness, the trial steering committee recommended that all deferred participants should be offered PrEP immediately.

PROUD also confirmed that PrEP was highly effective in a real world setting in a group of men engaging in sex with very high STI transmission risk. PROUD found no difference in the incidence of sexually transmitted infections in the two groups, including rectal gonorrhoea and chlamydia, despite a suggestion of risk compensation (more episodes of condomless anal sex) among PrEP recipients who had a high number of sexual partners. No serious adverse drug reactions were recorded; 28 adverse events, most commonly nausea, headache and aching joints, resulted in interruption of PrEP. In a population matching those recruited to the PROUD study, 13 men (90% CI 9-23) would need to access PrEP for 1 year to avert one HIV infection.

Scottish HIV PrEP SLWG for BBV and Sexual Health Executive Leads report can be accessed:
http://www.hivscotland.com/our-work/prep-in-scotland/scottish-reports-on-prep/

PROUD Study WWW.proud.mrc.ac.uk
HIV PrEP evidence
IPERGAY study – France and Canada

• This study reported a 86% reduction in a similarly high risk group of gay men and transgender women
• IPERGAY used ‘event based’* dosing rather than daily PrEP

*Event based Dosing (EBD) (also called ‘on demand’)
If people do not wish to take a daily pill there is an option to use PrEP when needed


Figure 4
Current position-HIV PrEP in Scotland

• In October 2016, the HIV PrEP Short Life Working Group reported to the Sexual Health and Blood Borne Virus Executive Leads regarding HIV PrEP in Scotland. They strongly recommended that people at the highest risk of HIV in Scotland are provided with the option of PrEP as part of a wider targeted national prevention programme.
  • On the 10th April, 2017, the SMC announced that Truvada® was now accepted for use within NHS Scotland as an HIV PrEP intervention.
  • From 1st November 2017 Dr Reddy’s (Emtricitabine / Tenofovir Disoproxil Succinate) is the recommended supplier/preparation for PrEP.
  • In agreement with stakeholders the provision of this service in specialist sexual health services was launched officially during July, 2017.

• At the 2nd November 2015 Sexual Health and Blood Borne Virus Executive Leads’ meeting, following a presentation by HIV Scotland, there was agreement to form a subgroup to provide recommendations to the Executive Leads on Initiatives and strategies relating to HIV PrEP in Scotland.
• This SLWG comprised of advisers from the community, third sector, drug procurement, epidemiology, pharmacy, sexual health clinicians, sexual health promotion leads, HIV clinicians, and academics to provide recommendations on initiatives and strategies relating to HIV and PrEP in Scotland.
Summary - Why introduce HIV PrEP in Scotland?

• Clinical trials show at least 86% reduction in HIV sexual transmission (PROUD and IPERGAY studies) using HIV PrEP
• RCTs in heterosexuals have also demonstrated efficacy with 77% reduction in TDF2 and 73% in partners in PrEP. The reduced efficacy in heterosexuals is thought to be due to lower drug levels in females and is under review with further research
• Potential to greatly reduce new HIV cases in those at the highest risk, in combination with other prevention methods (London steep fall clinics)
HIV PrEP implementation in NHS Scotland
HIV PrEP implementation in NHS Scotland

• HIV PrEP needs to reach individuals at the highest risk of acquiring HIV infection to be effective
• HIV PrEP has been SMC approved and needs to be implemented in the same way as other effective new interventions, including review of current practice and priorities
• In consultation with stakeholders it was agreed that the provision of this service in specialist sexual health services would be launched officially during July, 2017
• Practitioners should liaise with sexual health teams in their board area to confirm local arrangements
HIV PrEP implementation in NHS Scotland

Eligibility criteria
HIV PrEP - Universal criteria

- Aged 16 or over
- Tested HIV negative
- Able to attend the clinic for regular 3 monthly review including for monitoring, sexual health care and support and to collect prescriptions
- Willing to stop NHS funded PrEP if the eligibility criteria no longer applies
- Resident in Scotland

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Eligibility criteria

• Current sexual health partners, irrespective of gender, of people who are HIV positive and with a detectable viral load
• MSM and transgender women with a documented bacterial rectal STI in the last 12 months
• MSM and transgender women reporting condomless penetrative anal sex with two or more partners in the last 12 months, and likely to do so again in the next three months
• Individuals, irrespective of gender, at equivalent high risk of HIV acquisition, as agreed with another specialist clinician
HIV PrEP - Not eligible

- Already HIV-positive or suspected HIV seroconversion
- Monogamous serodiscordant couples where the HIV positive partner is on treatment and has undetectable viral load
- Pre-existing medical conditions (such as renal impairment) that significantly increase the risk of Tenofovir/FTC adverse events
- Individuals chronically infected with hepatitis B virus where Tenofovir/FTC may be used for therapy can still use HIV PrEP but should take daily PrEP and care should be in coordination with the local hepatology team. These patients should also be advised not to stop HIV PrEP without medical advice.
HIV PrEP – Current medication
Current medication

- From 1st November 2017 Dr Reddy’s (Emtricitabine / Tenofovir Disoproxil Succinate) is the recommended supplier/preparation for PrEP

*PEPSE - Post exposure prophylaxis following sexual exposure

From July to November 2017 the following was used:
Brand name for a fixed dose co-formulation of
  ➢ Tenofovir disoproxil fumarate (TDF)
  ➢ Emtricitabine (FTC)
Licensed for treatment of HIV as part of combination therapy
Widely used off-licence in PEPSE*

From 1st November 2017 Dr Reddy’s (Emtricitabine / Tenofovir Disoproxil Succinate) is the recommended supplier/preparation for PrEP.
HIV PrEP — side effects

- Majority of people do not report side effects

**Potential side effects**

- Nausea, diarrhoea, bloating and headache can happen in about 1 in 10 people in the first months but usually resolve.
- PrEP can affect kidney function and bone density and therefore monitoring is important.
- ‘Event based’ PrEP might reduce the risk of side effects as less drug exposure though this has not been formally studied yet.
**HIV PrEP-side effects (contd.)**

**Kidney function**
- A small proportion of people taking PrEP have developed reduced kidney function
- Changes to kidney function reversed when stopping PrEP
- Risk is higher in older adults and/or risk factors for renal disease such as nephrotoxic drugs or family history

**Bone Density**
- PrEP can reduce bone density by 1-5%
- This thinning of the bones reverses after PrEP is stopped
- Risk higher if you already have low bone density related to other factors
- To date there have been no reports of bone fractures relating to PrEP use
How is PrEP taken?

Trials have shown that PrEP can be taken in two ways:

1. Daily Dose

One pill everyday - for people who are at ongoing high risk of acquiring HIV
1. Daily PrEP: protection 24/7

- Most PrEP studies have used daily PrEP
- Taking PrEP every day helps ensure there are protective drug levels 24 hours a day, 7 days a week
- For people who routinely have sex more than once a week daily PrEP is likely to be a better dosing option
- Daily PrEP allows some flexibility in that missing an occasional dose is not likely to impact on effectiveness
1. Daily PrEP: protection 24/7

- It is unclear how many days are needed before PrEP becomes effective but current evidence suggests for daily dosing in MSM 7 days of pills should be taken before relying on it to prevent HIV infection.
- If an MSM starting daily dosing thinks they may be at risk before finishing the first week of PrEP then a starting double dose should be advised. This is not advised for non MSM.
- For heterosexual men and women and transgender men and women 7 days of pills is currently advised before relying on PrEP.
- If stopping daily PrEP MSM need to take at least 2 days of PrEP after their last sexual exposure and heterosexual individuals and transgender men and women need to take 7 days of PrEP.
2. Event based dosing (also called on demand)

- Advised when an individual is at risk of infection less frequently for example once per month, or who do not want to take a tablet each day

- Only advised for MSM

- If taken this way care must be taken regarding timing of doses to maximise the efficacy of PrEP in preventing HIV infection

- Taking PrEP before and after a risk is still very effective

- The ‘before’ sex dose is important to ensure that appropriate drug levels are present before exposure
MSM can use PrEP intermittent dosing (event-based dosing). Not applicable to heterosexual prevention.

1. **EBD**: If you have sex once a week

   **BEFORE SEX**
   - 2 PrEP tablets at least 1 hour & ideally 24 hours before sex

   **AFTER SEX**
   - 1 PrEP tablet* after the 1st
   - 1 PrEP tablet after the 2nd
   - = total of 3 tablets after sex
   - *2 hours before or after planned time of sex

   ![Diagram of PrEP dosing options]

If you think you might have sex on Friday or over the weekend, you would ideally take two pills on Thursday; lets say you took them at 10 pm.
Event based Dosing (EBD)

Event based dosing involves:

• Taking a double dose of PrEP (two pills) before having sex
• Ideally taken 24 hours before having sex, but can be effective between 2 and 48 hours
• Take a single pill 24 hours after the initial double dose and then every 24 hours until 2 days after last sex

Individuals should aim to have a single pill each day until two days after the last episode of sex

Note: No more than 7 doses should be taken per week unless advised by a registered health practitioner.
PrEP and drug resistance

- If a person becomes HIV positive, there is a small risk of developing drug resistance to one or both drugs.
- This means that these drugs may not work as well in future treatment for HIV if required.
- In PrEP studies, very few people became HIV positive whilst taking PrEP, and of these, 1 in 20 developed drug resistance which is lower than overall rate of HIV resistance in the UK (7.5% in 2015).
- Highest risk of drug resistance is if individuals start PrEP when they already have HIV or if they stop PrEP and their HIV status is not checked prior to restarting.

In February 2016, a case was reported of someone who became HIV positive even though they were taking PrEP correctly. This was as a result of them catching HIV from a partner who was already resistant to the drugs in PrEP. This is a very rare event. Currently, drug resistance to tenofovir and emtricitabine is very uncommon in the UK.

http://www.hivrdb.org.uk/hiv-drug-resistance-uk
PrEP and other STIs

- **PrEP will not** protect against other STIs- unless condoms are being used
- Generally STIs are manageable but can sometimes cause unpleasant symptoms, some of which can be serious
- Regular checks for STIs when taking PrEP is important, as is the use of condoms

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Does PrEP interact with any other medications?

- Tenofovir and Emtricitabine do not interact with many other medicines

**Tenofovir and non steroid anti-inflammatory drugs**

- One important interaction is between Tenofovir and non-steroid anti-inflammatory drugs, especially diclofenac. Together they can cause kidney problems
- Other medicines from this class include ibuprofen and naproxen
- Avoid using these medicines if you are using PrEP
- Further information can be found at [http://www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)

**Recreational drugs**

- PrEP does not react with other recreational drugs but if these effect kidney function they should not be taken at the same time as PrEP
Before starting PrEP

Registered practitioners should:

• Ensure an individual has a HIV test before starting PrEP
• PrEP cannot be used if someone is HIV positive
• A 4th generation HIV blood test should be used as it indicates HIV status 4 weeks ago
• Some near patient tests are 3rd generation and indicate HIV status 3 months ago. If using this test it is advised this is repeated before starting PrEP or to use a 4th generation test.
• Practitioners should ensure they are aware of what generation tests their clinics are using
Before starting PrEP (contd.)

• PrEP should not be started if a person has flu like symptoms and a recent HIV risk in order to rule out recent seroconversion
• Kidney function should be checked via a blood test for Creatinine prior to starting PrEP
Before starting PrEP (contd.)

- Check for other sexually transmitted infections
- Test for hepatitis B and recommend vaccination, or boost a previous vaccine as appropriate
- Hepatitis B positive individuals can still use PrEP but should use daily dosing and in coordination with hepatology
Routine monitoring

Registered practitioners should advise clients of the importance of regular review:

Every 3 months at the sexual health clinic
- HIV test - 4th generation or antigen/antibody HIV blood test
- Sexual Health screen
- A urine dipstick for protein, if there is more than a trace, a blood test for creatinine and bone profile and urine for protein creatinine ratio should be performed

Every 12 months
- Blood test for Creatinine
- This may be performed more frequently if other risk factors for renal disease
Other considerations

Practitioners should discuss any concerns individuals may have in relation to taking PrEP including:

- Eligibility
- Adherence
- Any new health issues including symptoms of seroconversion such as sore throat, myalgia, flu-like symptoms and rash
- New medications and exclude interactions
- Recreational drugs
- Relationship issues including pressures from other to take PrEP

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Resources

• Scottish Medicines Consortium

• BHIVA/BASHH statement on PrEP

• HIV Scotland
  http://www.hivscotland.com

• Other useful sites
  www.prep.scot
  www.s-x.scot
  www.waverleycare.org