West of Scotland: Protocol for HIV Pre-exposure Prophylaxis (PrEP)

Version 1 (December 2020)

BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis 2018:
https://www.bhiva.org/prEP-guidelines

Section 1: Introduction

Who is this guidance for?

This guidance is for staff working in specialist sexual health services in the West of Scotland to be able to:

- Understand what PrEP is, identify those who might benefit and who will not be likely to benefit
- Be able to provide accurate information to individuals requesting PrEP
- Be able to apply NHS funded PrEP eligibility criteria and discuss this with individuals
- Be able to provide baseline testing prior to starting PrEP
- Be able to monitor and clinically manage individuals taking PrEP medication

What is HIV PrEP?

PrEP is one of several ways of reducing sexual transmission of HIV (others include condom use or changes in behaviour). **PrEP medication should therefore be considered as just one component of wider interventions to prevent HIV transmission in those at highest risk.**

What is the evidence base for use of PrEP

In 2015 two studies (PROUD, UK and iPERGAY, France) reported efficacy in men who have sex with men (MSM) of 86%. Efficacy is linked to levels of adherence.
These studies used a combination of 2 oral antiretroviral drugs: Tenofovir disoproxil fumarate (TDF) and Emtricitabine (FTC). Several generic versions of Tenofovir disoproxil/FTC also exist.
PrEP is cost effective meaning that it is as cheap (or cheaper) to provide TD/FTC to high risk individuals as prevention than to treat the proportion who would go to acquire HIV infection.

Can PrEP be prescribed at specialist sexual health clinics in Scotland?

Yes. It is indicated for HIV negative adults who are at high and ongoing risk for HIV infection. Eligibility criteria must be applied.

Can people get PrEP from non-NHS sources?

- Some people choose to buy PrEP online at a cost of around £40 for each months supply. Information on how to do this is in the i-base guide http://i-base.info/uk-guide-to-prep/. The website www.iwantprepnow.co.uk also provides information about PrEP
- It is legal for a patient to purchase and import 3 months of generic drug via the internet for personal use

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Referring individuals to be seen

If an individual is considering NHS funded PrEP (or is already taking self-purchased PrEP) they should be booked into the appropriate clinic in your board for their initial assessment. The initial PrEP appointment should be for 40 minutes. If booking a client into clinic then **baseline investigations** as detailed on page 4 can be completed ahead of their appointment (if resources permit) to allow prescriptions to be completed at their first PrEP clinic appointment. An HIV test result from the previous 45 days is usually required before commencing PrEP.
Please see section 6 for follow-up arrangements.

Section 2: Establishing eligibility for NHS funded PrEP

Universal criteria

Before being assessed for eligibility for NHS funded PrEP, the individual must satisfy all of the following Universal criteria:

1. Be aged 16 years or over
2. Have a negative fourth generation HIV test in the preceding 45 days
3. Be able to attend for regular 3 monthly reviews for monitoring, sexual health care and support, and to collect prescriptions
4. Willing to stop NHS-funded PrEP if eligibility criteria are no longer met
5. Resident in Scotland

Eligibility criteria

If all of the above universal criteria are met, the client may be assessed for NHS funded PrEP. An individual is eligible for PrEP if one or more of the following apply:

1. Their current sexual partner(s) is HIV positive and has a detectable viral load
2. MSM & transgender women with a documented bacterial rectal STI in the last 12 months
3. MSM & 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 3 months
4. Individuals, irrespective of gender, at an equivalent high risk of HIV acquisition, as agreed with another specialist clinician

Exclusion criteria

PrEP should **not** be used:

- If the individual is already HIV-positive or in suspected HIV seroconversion
- In monogamous serodiscordant couples where the HIV+ partner is on treatment and has an undetectable viral load
- Pre-existing medical conditions that significantly increase the risk of Tenofovir disoproxil/FTC adverse events

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Section 3: Pre-PrEP work-up

Initial PrEP consultations

- Record "STI-PrEP" as the Main Reason for attending on episode page of NASH
  and write 'new' or 'continuing' in the *'notes'* box under the main reason for attending
- Complete HIV PrEP proforma (appendix 1) and paste into clinical note – name this clinical note: 'PrEP initial consultation'
- STISS code the episode – code all relevant options (Appendix 2)

Investigations required:

- 4th generation HIV test: A negative result must be obtained within 45 days preceding initiation of PrEP
- Hepatitis B cAb (or sAb to ensure vaccination response if not previously done)
- Hepatitis C Ab
- Syphilis serology
- Chlamydia and GC NAAT from all relevant sites
- Urinalysis (if urinalysis shows >++ proteinuria this needs further investigation before PREP is started (BP, UPCR, senior medical review)
- UPCR if >1+ protein on urinalysis
- U+Es
- Pregnancy test
- Weight
- Blood pressure
- Calculation of Creatinine clearance using the local recommended equation for measuring renal function such as CKD-EPI or MDRD or Cockcroft gault equation. It is important to use the same equation consistently to allow for comparison and assess any changes that should occur

Specific situations- Considerations prior to prep initiation

HIV window period

- Symptoms of Primary HIV Infection (PHI) – PrEP must not be provided until PHI excluded

Hepatitis B surface antigen positive

- Discuss with hepatology team prior to initiating Tenofovir disoproxil/FTC and prior to stopping
- If PrEP initiated then daily dosing regimen must be used
- If PrEP initiated – will need close monitoring of LFTs on interruption of PrEP
- Risk of resistance with poor adherence

Risk of renal toxicity is increased if:

- Pre-existing renal dysfunction
- Nephrotoxic drugs – including NSAIDS (such as ibuprofen and diclofenac), and recreational drugs
- Hypertension
- Other co-morbidities including cardiac disease, diabetes
- Baseline renal dysfunction or proteinuria
- Age >50

Risk of reduction in bone mineral density is increased if:

- Risk factors for osteoporosis eg: smoking, steroid use, low body weight

Drug interactions

- These must be checked on www.hiv-druginteractions.org (see Appendix 2 for screenshot example)

Pregnancy risk

- Tenofovir disoproxil/FTC is not licensed to be used in pregnancy
- Tenofovir disoproxil /FTC can be provided if risk of acquiring HIV in pregnancy is greater than risks associated with PrEP
- Tenofovir disoproxil/FTC is not known to be teratogenic or harmful in pregnancy in PrEP trials
- The risks and benefits of alternatives to PrEP should be discussed with pregnant or breastfeeding woman
- Tenofovir disoproxil/FTC is not known to alter efficacy of hormonal contraceptive methods

HIV serodiscordant relationship

- Offer to see the couple together and individually
- HIV consultant to discuss treatment as prevention (TasP)
- Discuss legal implications re: reckless exposure and document
- Consider genotypic resistance pattern of the person living with HIV's virus

Section 4: Counselling to support PrEP prescription

a) Establish patient's understanding of, motivation for and expectations of PrEP

- Clarify limitations of PrEP
- Establish patient's commitment to follow-up and adherence

b) Discuss adherence and how to take medication

- Clarify that adherence is important in all to prevent drug resistance developing. Taking PREP as event based can be more complicated to understand so it is important to discuss this at every visit

c) Management of side-effects

- Supportive advice for mild side effects: headache, nausea, diarrhoea, bloating. Usually stops after approximately 1 month. Occurs in fewer than 10%.
- Seek urgent medical advice if develops rash or symptoms of allergy
- The most serious side effect is the potential for renal toxicity, particularly in those aged over 40 and/or with pre-existing kidney issues
- Bone health: 1.5-2% reduction bone mineral density at hip and spine at 48 weeks

d) Counsel around nephroxicity

- Advise against NSAID use
- Advise to check drug-drug interactions for all prescribed/OTC and herbal remedies
- Counsel around avoiding dehydration with recreational drug/alcohol use
- Note that the use of creatinine supplements may affect eGFR but are not contraindicated with PREP

e) Counsel around risk of HIV infection and primary HIV infection (PHI)

- Re-enforce importance of adherence
- Discuss PHI symptoms and need to test urgently for HIV if symptoms develop; Discuss small risk of anti-retroviral resistance if acquires HIV
- Discuss combination prevention strategies – condom use

f) Counsel around management of missed doses (see section 7)

g) Counsel around plans to discontinue (see section 8)

h) Arrange follow-up (see section 6)

Section 5: PrEP prescribing and dosing options

The number of tablets prescribed at the first visit should be **90 tablets** for those who have no comorbidities or other concerns and who were not within the window period at initiation.

If the person is within the window period for HIV when they start they should only get **enough tablets to cover this period and allow further testing**.

Medication must be prescribed on NASH.

Subsequent supplies will usually be for 3 months (90 tablets).

Six month supplies can be given to those who are <40yrs old and have been on PREP for a minimum of 6 months and are stable. They still need to have 3 monthly screens (At 3 months it is key to Test for HIV, Syphilis, Chlamydia and Gonorrhoea**)**

Tenofovir disoproxil /FTC can be provided as daily dosing or event-based dosing (EBD). These are differentiated on the prescription page of NaSH.

Daily and event-based PrEP showed similar efficacy in MSM so either may be offered to MSM.

Daily dosing

- One dose is taken every day, ideally at the same time every day, regardless of sexual activity
- Most evidence exists for daily dosing
- Can be used by any patient regardless of gender or risk group
- **Only** option for people with Hepatitis B infection
- Does not require forward planning
- Ideal for individuals who have frequent sex (weekly)
- Should be taken at the same time every day
- More forgiving of missed doses once steady state achieved
- Disadvantages include higher exposure to possible toxicity and higher drug costs
- Consider starting with a double dose if imminent risk
- Takes 2-24 hours to be effective in msm for anal sex **after taking a double dose**. The time to clinical protection is estimated as 7 days for insertive and receptive vaginal sex, and 7 days for injecting drug use

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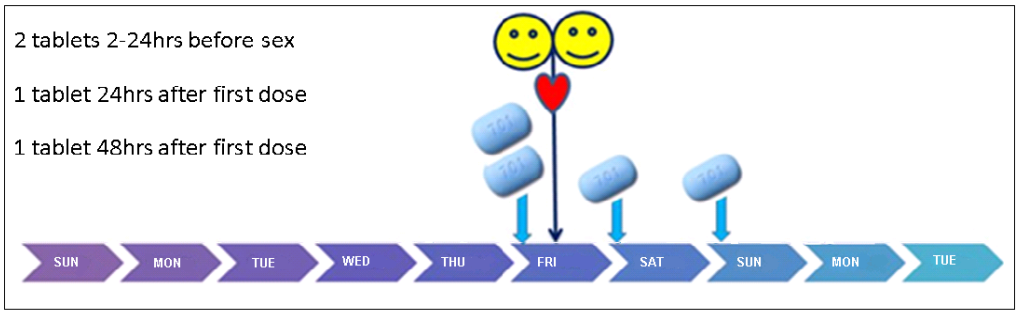
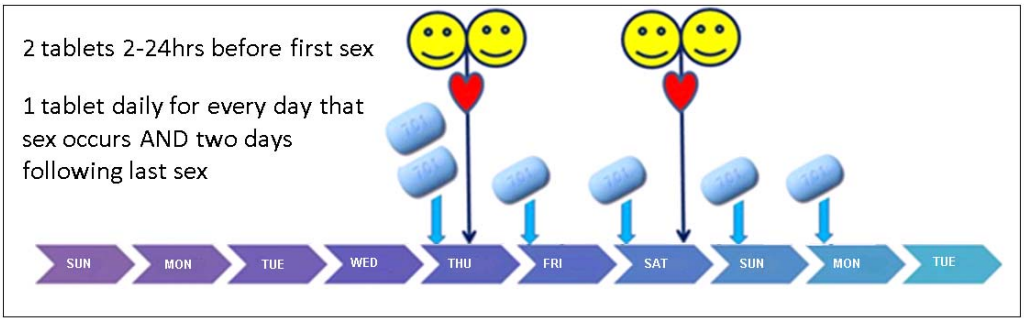
Event-based dosing (EBD)

- Not to be used by heterosexual or trans individuals
- Not for those with active Hepatitis B infection
- Requires forward planning
- Ideal for people who have less frequent sex (less frequently than weekly) as more than 7 doses per week is not recommended
- Less forgiving if missed doses
- Advantages include lower exposure to possible toxicity and lower drug costs
- Event-based dosing for a single sex act of condomless anal sex requires 2 tablets of Tenofovir disoproxil/FTC 2-24 hours before sex, 1 tablet 24 hours (22-26 hours) after the first dose, and another tablet 48 hours (46-50 hours) after the first dose

Single risk dosing:



Multi-risk dosing:



Section 6: Follow-up

Timing of follow-up depends on the need for HIV testing after the window period. The majority of patients on PrEP can have an email or telephone communication towards the end of the first month of PrEP use (regardless of dosing schedule) and 3 monthly attendances thereafter. Medical review at 3 months and 12 months (and every 12 months thereafter) for all.

Who needs to attend in person for a 6 week appointment? (Also known as 'end of window period' appointment)

Those within the window period when starting PREP or those who have increased risk of renal dysfunction.

The following should be done at this face to face appointment.

6 week/ 'end of window period' appointment:

- HIV test
- Discuss side-effects
- Adherence check and support
- Pregnancy test if indicated
- Urinalysis (UPCR if ≥ 1+ proteinuria)
- Provision of further PrEP supply (if only received 30 days initially)
  - Daily dosing – 1 tab daily 90 days
  - EBD – 1 tab as directed (30-90 tablets depending on use)
- Arrange follow-up appointment for 3 months

For those who are having a telephone or email 1 month follow-up:

The 1-month consultation should preferably be via email and cover adherence and side effects and ensure the appointment for 3 months is in place. This 1 month consultation should be done via the virtual clinic tab. Ensure email address and permissions at initial appointment. Record in NASH that email has been sent

Who should do further follow up:

Nurse Prescriber review at 6,9 months (then 15,18,21 months) for those with no co-existing renal/bone/cardiac conditions; no proteinuria; CrCl>70; no drop in renal function; no drug interactions. Medical review at 3 months and 12 months (and every 12 months thereafter) for all.

What to do at 3 or 6 monthly review appointments (see proforma on page 13):

- Adherence check and support
- HIV test
- STI screen – Syphilis; Chlamydia/GC for all relevant sites; Hepatitis C (if risk factors)
- Pregnancy test if indicated
- Urinalysis (UPCR if ≥ 1+ proteinuria)
- Discuss chemsex
- Enquire about any new medications/ supplements and check for new interactions
- U+E should be checked 3 monthly for patients identified as high renal risk: concomitant meds; proteinuria; abnormal at baseline); 6 monthly U+E for those >40 yrs or CrCl 60-90ml/min and 12 monthly for those <40yrs
- Provision of further PrEP supply
- Arrange follow-up appointment for 3 months
- Write to GP (letter proforma on nash)

Annual 12 monthly review (see proforma on page 14):

- Routine 3 monthly review as above
- U+E
- Review ongoing HIV risk factors and eligibility for PrEP
  - Patient remains eligible - provide further PrEP and arrange 3 month follow-up
  - Patient no longer eligible - proceed to **section 8**

Section 7: Adherence and management of missed doses

The time to achieve a protective concentration is determined by the drugs used, the dose and the frequency of dosing and the target tissue.

Daily dosing

It takes 7 days after starting for levels to be protective. After 2 weeks of daily dosing (MSM)and 3 weeks (women) levels are steady state and missed doses are less of a concern.

2-24 hours for clinical protection for anal sex after a double dose. The time to clinical protection is estimated as 7 days for insertive and receptive vaginal sex. Missed doses after this time are less of a concern.

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If the patient has missed ≥ 7 consecutive days

If no UPAI in previous 72h

- Review previous adherence and need for definitive HIV testing
- If restarting daily PrEP then consider double dose to start if imminent risk

If UPAI in previous 72h

- Discuss POST exposure prophylaxis (PEP) depending on risk
- If PEP not given, consider definitive HIV testing before re-starting PrEP
- If re-starting PrEP immediately then consider double dose to start if imminent risk

On demand/ Event-based dosing

No steady state is reached in the blood and missed doses may become more problematic

- If the pre-sex dose is missed then the patient should take two tablets as soon as possible and seek advice – discuss with GUM Consultant
- If any subsequent doses are missed then discuss with GUM Consultant
- If frequent missed pills then consider daily dosing
- If restarting on demand prep less than 4 days after last dose restart with a single dose. If four or more days since last dose restart with a double dose

Section 8: Discontinuing PrEP

- Formally assess continuing eligibility, willingness and ability to adhere at each annual visit or outwith this timeframe if there is thought to be any significant change in a client's risk
- Discontinue NHS funded PrEP if:
  - Universal criteria are no longer all met
  - None of the eligibility criteria apply
  - Any exclusion criteria are met

- If a patient is no longer eligible for NHS funded PrEP, but wishes to continue on self-funded PrEP they would still be eligible to attend the PrEP clinic for monitoring
- Ensure no active Hepatitis B infection
- Patients with Hepatitis B should only discontinue PrEP after discussion with GUM consultant.
- PrEP should continue for 48h following most recent anal sex or for 7 daily doses if vaginal sex

- HIV testing should be done 4 weeks following most recent risk
- Continue to provide routine sexual health care, condoms and advice about PEPSE
- PrEP can be re-started again if circumstances change

Section 9: Managing patients not eligible for NHS funded PrEP

Patients who do not meet the criteria but wish to start PrEP should have a discussion which includes the following:

- That the patient is not at greatest risk of acquiring HIV and this is reassuring
- That PrEP may not add much additional protection to existing risk reduction strategies
- That the risks of harm may outweigh potential benefit
- That the patient can still access regular STI/BBV screening and PEPSE
- That the patient may be eligible for PrEP in the future if risk changes
- That the patient may wish to self-fund Tenofovir disoproxil/FTC via online site via www.iwantprepnow.com

  Patients who choose to self-fund can access routine monitoring from specialist sexual health clinics:
- The monitoring programme is identical to those accessing NHS-funded PrEP
- Patients should have a pre-PrEP work-up
- Patients should have a discussion with a GUM consultant with results of the pre-PrEP work-up
- Provide the ***i-base*** booklet Scotland PrEP Guide: Buying PrEP online:

  www.I-base.info/prep-in-scotland-guide/

Appendix 1[1]: PREP proforma initial assessment

- **Date**:
- **Person completing form**:

Universal criteria met		
Eligibility criteria – identify (1-4)		
Any exclusion criteria present		
Date of last HIV test: result		
Hepatitis B status and date **(bloods + vaccination)**		
Increased risk of kidney disease: **Calculated Creatinine Clearance:** **Urinalysis/ UPCR:** **Weight:** **BP:**		
Increased risk of bone disease		
Last UPAI		
Number of condomless AI partners in last 12/12		
Discussion/ support other risk reduction methods		
Consent to contact GP – initiation and annually		
Daily or event based dosing		
STISS coding		
Follow-up: **1 month telephone or 3 month clinic**		

Appendix 1[2]:PREP proforma 3 and 6 month visit

- **Date**:
- **Person completing form**:

	Result
HIV test	
SHS (and Hep C serology if risk factors)	
Reason for continuing	
Adherence discussed	Yes/No
If Increased risk of kidney disease or >50yrs: **Calculated Creatinine Clearance:**** **Urinalysis/ UPCR:**	
Discussion/ support other risk reduction methods	Yes/ No
Aware of symptoms of Acute HIV infection	
Daily or event based dosing	
STISS coding	
Follow-up –3 or 6 month/ Nurse or Dr	

****creatinine clearance to be done 6 monthly in those over 40 years and 12 monthly in those under 40 years old**

Appendix 1[3]:PREP proforma 12 month visit

- **Date**:
- **Person completing form**:

	Result
Eligibility criteria – identify which (1-4)	
Any exclusion criteria present	
Date of last HIV test with result	
Hepatitis B status and date **(bloods + vaccination)**	
SHS and Hep C serology	
Increased risk of kidney disease: **Calculated Creatinine Clearance:** **Urinalysis/ UPCR:** **Weight:** **BP:**	
Increased risk of bone disease	
Adherence	
Aware of symptoms of acute HIV infection	
Number of condomless AI partners in last 12/12	
Discussion/ support other risk reduction methods	
Consent to contact GP – annual letter	
Daily or event based dosing	
STISS coding	
Follow-up – Nurse or Dr	

Appendix 2: Coding and HIV drug interaction screenshots