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

Version 2 (July 2024)

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
- Provide accurate information to individuals requesting PrEP
- Understand the original NHS funded PrEP eligibility criteria
- Provide baseline testing prior to starting PrEP
- Monitor and clinically manage individuals taking PrEP

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.** Most individuals will be prescribed oral Tenofovir Disoproxil/Emtricitabine (TD/FTC) as PrEP. A small minority of patients will be prescribed Tenofovir Alafenamide/Emtricitabine (TAF/FTC) (see section 9).

PrEP reduces the risk of getting HIV **from sex** by about 99% when taken as prescribed.

People who 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:
  https://i-base.info/guides/prep/buying-prep-online
- The website www.iwantprepnow.co.uk also provides information about PrEP
- **Can still access routine monitoring from sexual health clinics**

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. 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.

Section 2: Establishing eligibility for NHS provided PrEP

Universal criteria

Before being assessed 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 baseline HIV test
3. Be able to attend for regular 3 monthly reviews for monitoring, sexual health care and support, and to collect prescriptions
4. Resident in Scotland

Eligibility criteria

Scottish services are moving away from using specific eligibility criteria. PrEP is suitable for most people who request it, except where HIV risk is very low and therefore the risk of PrEP outweighs the benefit.
If all of the above universal criteria are met, the following are the original eligibility criteria that should still be used as a guide.

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 (see below for examples)

The following are examples of indicators that someone may benefit from PrEP under category 4 above and should prompt discussion around PrEP:

- MSM who may have condomless anal sex in the future
- People who have chemsex or group sex
- Women who have bisexual male partner(s)
- People from high prevalence countries (eg: Sub-Saharan Africa)
- People who tend to have partners from high prevalence countries
- People who have transactional sex
- People who inject drugs or whose partner(s) inject drugs (PrEP for injecting risk alone is currently off licence in Scotland. Discuss these cases with senior medical staff)

Exclusion criteria

PrEP should **not** be used:

- If the individual is already HIV-positive or in suspected HIV seroconversion
- In monogamous sero-discordant couples where the person living with HIV is on treatment and has an undetectable viral load for more than 6 months

Section 3: Pre-PrEP work-up

Initial PrEP consultation

- Create a new episode in NASH
- Record "STI-PrEP" as the Main Reason for attending on episode page of NASH
- Complete the '***HIV PREP ASSESSMENT'*** form on nash
- STISS code the episode – code all relevant options (Appendix 2)

Baseline Investigations required:

- 4th generation HIV test
- 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 discussion with senior medical staff before PREP is started
- UPCR if >1+ protein on urinalysis
- U+Es
- Pregnancy test
- Consider Blood Pressure if other concerns or clinically indicated
- Calculation of Creatinine clearance using the local recommended equation for measuring renal function such as CKD-EPI. It is important to use the same equation consistently to allow for comparison and assess any changes that should occur. This is recorded on the HIV '*HIV prep assessment'* form

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/recent history of Hepatitis B infection

- Ensure you have up to date Hepatitis B results before starting PrEP
- If Hepatitis B sAg is positive discuss with hepatology team prior to initiating PREP AND prior to stopping (LFTS will need close monitoring on stopping)
- If PrEP initiated then daily dosing regimen must be used

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 >40

Risk of reduction in bone mineral density is increased if:

- Risk factors for osteoporosis eg: smoking, steroid use, low body weight
- In those over 50 years, risk factors for reduced bone mineral density should be assessed at baseline, the FRAX tool could be undertaken to indicate the need for a DEXA scan

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 as PREP
- 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 method

HIV serodiscordant relationship

- Offer to see the couple together and individually
- HIV specialist to discuss treatment as prevention (TasP) and Undetectable = Untransmissable (U=U)

- Consider genotypic resistance pattern of the person living with HIV if detectable viral load
- See section 2: Exclusion Criteria

Section 4: Counselling to support PrEP prescription

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

- Clarify limitations of PrEP e.g. it is only effective against risk of HIV transmission, it does not protect against other STIs, and must be taken as prescribed to be effective
- 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 ensure efficacy. Taking PREP as event based can be more complicated to understand so it is important to discuss this regularly

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 worsening 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 creatine supplements may affect eGFR but are not contraindicated with PREP. The recommendation is to stop for 7 days before kidney function is tested, but this is a pragmatic approach rather than being evidence based

e) Counsel around risk of HIV infection and symptoms of 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)

i) Offer to send link to HIV PREP leaflet via SMS sender (leaflet link accessed through link on '*HIV PREP assessment*' form

Section 5: PrEP prescribing and dosing options

The number of tablets prescribed at the first visit should usually be **120 tablets** (3 months plus one month buffer) 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 get **enough tablets to cover this period and to ensure further timely testing**.

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

Subsequent supplies will depend on how much the individual has:

- Ensure those coming for 3 month clinical review have enough to allow for appointment changes (usually 4 months)
- **Six or seven month supplies can be given to those who have been on PREP for a minimum of 3 months, are stable and are categorised as green/ amber (see page 10) . They still need to have 3 monthly sexual health testing (**HIV, Syphilis, Chlamydia and Gonorrhoea**)**

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

Daily dosing and time to clinical protection

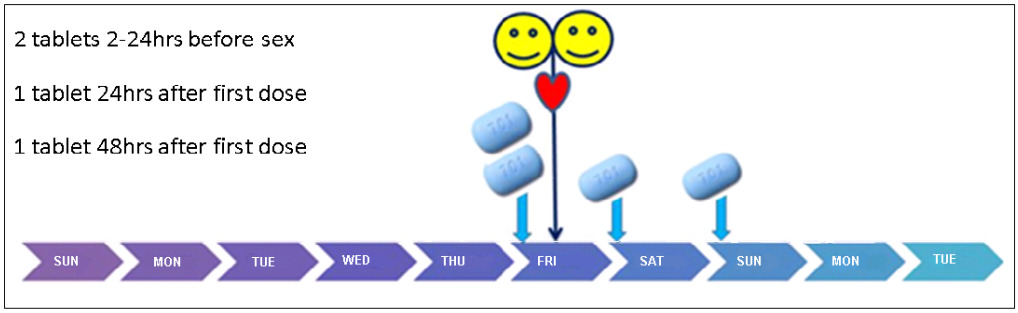
- One dose is taken every day, ideally at the same time every day, regardless of sexual activity
- Most evidence exists for daily dosing
- Can be used by any patient regardless of gender or risk group
- **Only** option for people with Hepatitis B infection
- Does not require forward planning
- Ideal for individuals who have frequent sex (weekly)
- 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
- The time to clinical protection is estimated as 2-24 hours to be effective in msm for anal sex **after taking a double dose OR 7 days if no double dose**
- The time to clinical protection is estimated as 2-24 hours to be effective in men having insertive vaginal/frontal sex **after taking a double dose OR 7 days if no double dose**
- The time to clinical protection is estimated as 7 days to be effective in women/transmen for insertive and receptive vaginal sex, double dosing **IS NOT** recommended for women and transmen for vaginal/ frontal sex
- The time to clinical protection is estimated as 7 days to be effective in those at risk from injecting drug use

Event-based dosing (EBD)

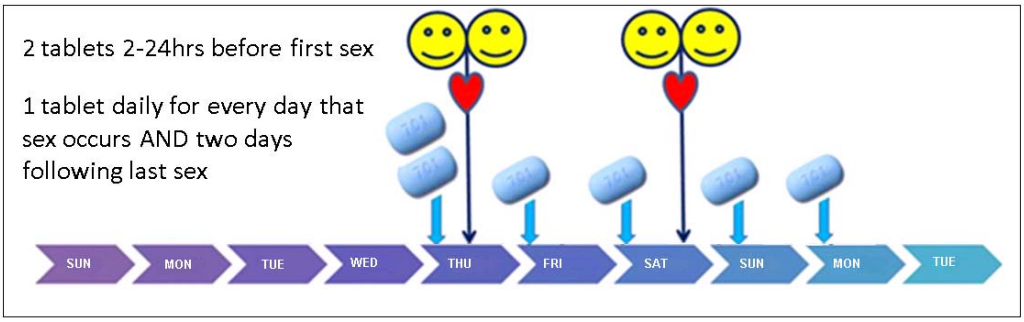
- Not to be used for protection for women/ transmen for vaginal/frontal sex
- Not for those with active Hepatitis B infection

- 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 2-24 hours before sex, then
    - 1 tablet daily continuously until last condomless anal sex, then
    - For 2 further days

PREP dosing if single sexual risk exposure:



Multi-risk dosing:



Section 6: First Follow-up after starting PrEP

Timing of initial follow-up depends on the need for HIV testing if they are within the window period when they commence PREP.

The majority of patients will attend at 3/12 for initial follow up.
Those who were in the window period when they started PREP should have an HIV test 45 days after the risk.

Subsequent follow-up
Depends on the categorisation of patient, as **Green, Amber** or **Red**, as follows:

GREEN:
Aged 18-40 years
No medical conditions which increase bone/renal risk
Maximum 1+ protein in urine (or UPCR <20)
No co-prescribed medicines which interact or associated with renal impairment
No significant social complexity

Follow-up: 6 monthly PrEP reviews with 3 monthly HIV/STI screens in between. Annual renal function/urinalysis

AMBER:
Aged >40 years and <70 years
GFR >60 < 90
Comorbidity which can impact kidneys/co-prescribed medication which can affect kidneys
No significant social complexity

Follow-up: 6 monthly PrEP reviews with 3 monthly HIV/STI screens in between. **Six monthly** renal function/urinalysis

RED:
Aged over 70 years
Aged under 18 years
eGFR < 60
Significant drop in eGFR (*see page 15- good practice points in reduction in creatinine clearance*)
uPCR > 30
Individuals with significant renal comorbidities (eg transplant)
Individuals with Hep B or C coinfection
Individuals with possible adverse reactions to PrEP
Individuals with reduced bone density (osteopenia/osteoporosis) or significant risk factors (previous fractures/alcohol/steroid)
Concerning drug interactions

Pregnant individuals
Significant social complexity
On TAF

Follow-up: 3 monthly PrEP reviews and **3 monthly** renal function/urinalysis

ONGOING investigations required whilst taking PrEP

Test	GREEN	AMBER	RED
Syphilis	Every 3m	Every 3m	Every 3m
HIV 4th generation	Every 3m	Every 3m	Every 3m
CT/GC NAAT at appropriate sites	Every 3m	Every 3m	Every 3m
Pregnancy test	As indicated by history	As indicated by history	As indicated by history
HCV Ab/PCR*	Annual	Annual	Annual
HBV cAb/ HBV sAg	As per local protocol	As per local protocol	As per local protocol
U+E	Annual	Every 6 months	As per clinician
Urinalysis	Annual	Every 6 months	Every 3 months
uPCR	If urinalysis protein 1+ or more	If urinalysis protein 1+ or more	If urinalysis protein 1+ or more
BP		As indicated	As indicated
Weight		As indicated	As indicated

**If history of chems/ group sex consider 3 monthly Hepatitis C*

What else needs to be done at the 3 or 6 monthly review appointments:

- Open an new episode and new '*HIV PREP assessment*' form for each review
- Adherence check and support
- Discuss chemsex
- Enquire about any new medications/ supplements and check for new interactions
- Provision of further PrEP supply
- Arrange follow-up appointment

- Ensure GP aware if consent

Annual 12 monthly review:

- Open a new episode and new '*HIV PREP assessment*' form
- Review ongoing HIV risk factors and need for PrEP
  - Patient no longer requires PrEP - proceed to **section 8**

Section 7: Adherence and management of missed doses

DAILY DOSING

Once PrEP is taken continuously for 7 days then there is still protection if the occasional dose is missed. For anal sex you need to take at least 4 doses per week. For vaginal/frontal it's at least 6 doses per week.

The following advice applies if:

a. The patient has missed ≥ 7 consecutive days, OR
b. Is having anal sex and taken fewer than 4 doses in the last 7 days, OR
c. Is having vaginal/ frontal sex and taken fewer than 6 doses in the last 7 days or more than 48 hours has elapsed since last dose

If no unprotected sex in previous 72h

- Review previous adherence and need for definitive HIV testing
- RESTART prep again
- Test as appropriate given window periods

If unprotected sex in previous 72h

- Consider POST exposure prophylaxis (PEPSE) depending on risk
- If PEPSE not given, consider definitive HIV testing before RESTARTING PrEP

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 senior medical staff
- If any subsequent doses are missed then discuss with senior medical staff
- 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

- A clinician should only recommend stopping PrEP when the risks outweigh the benefits
- If patient has significant bone/renal disease or has had toxicity from standard PrEP, TAF/FTC PrEP (Descovy) should be considered
- Patients with Hepatitis B should only discontinue PrEP after discussion with senior GUM clinician and hepatology team.
- PrEP should continue for 48h following most recent anal sex or for 7 daily doses if vaginal sex

Eligibility criteria for Tenofovir AF/Emtricitabine (Descovy®) for pre-exposure prophylaxis for HIV (PrEP) in Scotland

Tenofovir AF/Emtricitabine (Descovy® or TAF/FTC) has been shown to be non-inferior to Tenofovir DF/Emtricitabine (TDF/FTC) in reducing incident HIV infections in a large, randomised clinical trial involving gay, bisexual and other men who have sex with men (GBMSM) and transgender women (TGW). Adverse effects on markers of bone mineral density and renal function were significantly reduced in the Descovy® arm.

There is a significant cost implication in prescribing this regimen in place of generic TD/FTC, although the original cost benefit analysis supporting PrEP in Scotland was made using a list price for TDF/FTC PrEP (Truvada®) equivalent to the current list price for Descovy®.

For patients where Descovy® is being considered as PrEP, the case must be discussed at a local or regional HIV/GUM MDT. Where it offers comparable levels of risk reduction for the individual, event based or interval (‘holiday’) dosing of generic Tenofovir D/Emtricitabine should be trialled where possible.
In cases where indications are not clear, referral for discussion at the Scottish national complex PrEP MDT should be made and the decision documented and recorded.

The following scenarios may warrant consideration of starting or switching to Descovy® PrEP in individuals who fulfil Scottish Government PrEP eligibility criteria:

1. RENAL

a. High risk renal factors for TD/FTC:

Moderate or severe reduction in glomerular filtration (estimated glomerular filtration rate [eGFR] ≤ 59 ml/min/1.73m2 at baseline or during follow-up) and clinical assessment suggests that TAF/FTC would have a lower risk profile than TD/FTC

OR

- Individuals with proven renal toxicity[i] with TD/FTC (acute or chronic)

b. Medium risk renal factors for TD/FTC:

Individuals with an eGFR ≥ 60 ml/min/1.73m2 in which:

- a progressive reduction in estimated glomerular filtration rate on TD/FTC is seen

AND

- significant concurrent medical issues or monitoring/prescribing concerns that suggest TAF/FTC would have a lower risk profile to TD/FTC

2. BONE:

a. High risk bone factors for TD/FTC:

Individuals with confirmed osteoporosis on DEXA or a high risk of a major fracture as determined by an appropriate fragility risk score.
Note: high fracture probability defined as > 10% (major osteoporotic or hip fracture absolute risk), with NICE recommending QFracture or FRAX scores

b. Medium risk bone factors for TD/FTC:

Individuals who are < 18 years.
Note: markers of increased absolute fracture risk include previous vertebral fracture(s), high alcohol intake, high-dose oral or high-dose systemic glucocorticoids (more than 7.5 mg prednisolone or equivalent per day for 3 months or longer) or other causes of secondary osteoporosis

3. Gastrointestinal intolerance/swallowing difficulties:

There is no evidence base for changes made for GI intolerance, nor any evidence that Descovy® PrEP has better GI tolerability than TD/FTC PrEP. Any changes should be based on clinical experience and with MDT input. A list of excipients for all available TD/FTC formulations is available.

When not to use Descovy®

Descovy® should not be used in following circumstances:

- Individuals < 35 kg
- In those currently prescribed/taking: adefovir disoproxil, carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone or St John's Wort

Note: adefovir is also contraindicated with TD/FTC.

Caution should be used with patients with or at risk of metabolic and lipid disorders due to potential increase in lipid profile.
There are currently no completed clinical trials of the use of TAF/FTC for vaginal sex in cisgender women, but there is pharmacokinetic evidence to suggest that TAF can be expected to be non-inferior to TDF for all PrEP users. Where TAF is indicated for the reasons listed above, there is no reason to avoid TAF in any patient group. Dosing should be as per BHIVA guidelines.

SECTION 10: *Good practice points when there is a reduction in Creatinine Clearance/ proteinuria*

- Any reduction in eGFR of clinical concern should be confirmed at least once on a repeat sample before changing dosing or preparation, after confirming that any creatine and protein supplements have been discontinued
- A confirmed reduction of 15mL/min/1.73m2 **OR** 25% in eGFR from baseline to 60–69mL/min/1.73m2 is an indication for consideration of a non-TD PrEP (alternative TD/FTC PrEP dosing may be considered)
- A confirmed reduction of 15mL/min/1.73m2 or 25% in eGFR from baseline to 70-89 mL/min/1.73m2 is an indication for 3 monthly recheck of eGFR and consideration of alternative TD/FTC PrEP dosing
- If there is proteinuria on urinalysis, ensure sample is midstream
    - If +protein – send urine for UPCR
    - If ++/+++protein – check BP, UPCR, await result before commencing PREP
    - If blood/glucose on urinalysis, seek senior advice

Appendix 1: Coding and HIV drug interaction screenshots