HIV Post -Exposure Prophylaxis (PEP) Pathway

When to use PEP

- PEP is recommended where there is a **significant risk** of HIV transmission
- Risk-benefit analysis should be undertaken for every individual following an exposure and should include the:
    - ✓ Risk of the source being HIV-positive
    - ✓ Risk of transmission according to exposure and
    - ✓ HIV viral load (VL) in the source, if known
- Decision to initiate PEP should be made on a **case-by-case basis**
- Certain factors may increase the risk of HIV transmission and must be considered and discussed in a PEP consultation (see **box 1**)
- PEP prescribing recommendations are summarized in **Table** 1
- **PEP should not be considered or encouraged as a first-line method of HIV prevention – PEP should be integrated into counselling around safer sex strategies**

BOX 1: FACTORS INCREASING RISK OF HIV TRANSMISSION
1. **High plasma HIV VL in the source** 2. **Breaches in the mucosal barrier** e.g., mouth or genital ulcer disease, anal or vaginal trauma following sexual assault or first intercourse 3. **Menstruation or other bleeding** – theoretical risk only 4. **Sexually transmitted infections** in HIV positive individuals not on ART or HIV negative individuals with genital ulcer disease 5. **Pregnancy or postpartum** – per-act probability of HIV acquisition higher in late pregnancy and the postpartum period as compared to that during the non-pregnant period

TABLE 1: PEP PRESCRIBING RECOMMENDATIONS

	Index HIV Positive		Index of unknown HIV status	
	HIV Viral Load unknown or detectable	HIV Viral Load undetectable	From high prevalence country / risk-group (e.g. MSM) [a]	From low prevalence country / group
SEXUAL EXPOSURES				
Receptive anal sex	Recommend	Not recommended [b]	Recommend	Not recommended
Insertive anal sex	Recommend	Not recommended [b]	Consider [c,d]	Not recommended
Receptive vaginal sex	Recommend	Not recommended [b]	Generally not recommended [c,d]	Not recommended
Insertive vaginal sex	Consider [c]	Not recommended	Generally not recommended [c,d]	Not recommended
Fellatio with ejaculation	Not recommended	Not recommended	Not recommended	Not recommended
Fellatio without ejaculation	Not recommended	Not recommended	Not recommended	Not recommended
Splash of semen into eye	Not recommended	Not recommended	Not recommended	Not recommended
Cunnilingus	Not recommended	Not recommended	Not recommended	Not recommended
OCCUPATIONAL AND OTHER EXPOSURES				
Sharing of injecting equipment	Recommended	Not recommended [b]	Generally not recommended	Not recommended
Sharps injury	https://www.kura.gov.mt/Applications/Public/InfoCentre/Docs/OpenPost.aspx?WsAppId=444&Post=GrOmu716wKFr12Q			
Mucosal splash injury				
Human bite	Generally not recommended [g]	Not recommended	Not recommended	Not recommended
Needlestick from a discarded needle in the community	Not applicable	Not applicable	Not recommended	Not recommended

Recommended: the benefits of PEP are likely to outweigh the risks, PEP should be given unless there is a clear reason not to.
Consider: the risk of HIV transmission is low, the risk / benefit balance of PEP is less clear. The risk should be assessed on a case-by-case basis taking into consideration factors shown in footnotes c and d below.
Generally not recommended: the risk of HIV transmission is very low, the potential toxicity and inconvenience of PEP is likely to outweigh the benefit unless there is a clear specific extenuating factor which increases the risk (see footnotes c, d, e, f below). We anticipate PEP should very rarely be given when the risk has been assessed and discussed
Not recommended: the risk of HIV transmission is negligible and PEP should not be given

[a] High prevalence countries or risk-groups are those where there is a significant likelihood of the index case individual being HIV-positive. Within the UK at present, this is likely to be MSM, IDUs from high-risk countries (see d below) and individuals who have immigrated to the UK from areas of high HIV prevalence, particularly sub-Saharan Africa (high prevalence is >1%). HIV prevalence country specific HIV prevalence can be found at https://aidsinfo.unaids.org

[b] The index case has been on ART for at least 6 months with an undetectable plasma HIV viral load at the time of last measurement and within the last 6 months) with good reported adherence. Where there is any uncertainty about HIV VL results or adherence to ART then PEP should be given after condom less anal intercourse with an HIV-positive person. The viral load threshold considered 'undetectable' in the PARTNER 1 and 2 and HPTN052 studies was <200 copies/ml.

[c] Factors that influence decision-making in all exposures: More detailed knowledge of local HIV prevalence within index case population [a]

[d] Factors that may influence decision-making include in sexual exposures:
1. Breaches in the mucosal barrier such as genital ulcer disease and anal or vaginal trauma following sexual assault or first intercourse
2. Multiple episodes of exposure within a short period of time e.g. group sex
3. Sexually transmitted infection in either partner

[e] HIV prevalence amongst IDUs varies considerably depending on whether there is a local outbreak and country of origin and is particularly high in IDUs from Eastern Europe and central Asia. Region-specific estimates can be found in the UNAIDS Gap Report http://www.unaids.org/sites/default/files/media_asset/05_Peoplewhoinjectdrugs.pdf.

[f] Factors that may influence decision-making include in occupational exposures: Deep trauma or bolus of blood injected

[g] PEP should only be considered after a bite if all three criteria are met: a) the biter's saliva was visibly contaminated with blood; b) the biter is known or suspected to have a plasma HIV viral load >3.0 log copies/ml; c) the bite has resulted in severe and/or deep tissue injuries

PEP Post occupational exposure in Health Care Settings

- Refer to Infection Control Department of MDH

PEP Post-Sexual Assault

- Refer to ED of MDH or GGH [Females are to be referred to Obs and Gynae; Males will be treated at ED]

PEP after non-occupational exposure including consensual sex

Recommended combination
Emtricitabine/Tenofovir disoproxil fumarate 200mg/245mg one tablet daily
+
Raltegravir 400mg 12 hourly
Or
Dolutegravir 50mg once tablet daily
Or
Lopinavir/ritonavir 200/50mg two tablets 12 hourly

- A full 4-week course of PEP can be prescribed by all medical practitioners. ED is not the appropriate place for attendance for PEP prescriptions.

- PEP for non-occupational exposure must be procured privately by the patient (against payment). List of private pharmacies where above anti-retroviral drugs can be bought can be accessed through this link https://govmt.sharepoint.com/:w:/s/cpgmdh/EY48RRh8iCZGg2XzJ6xZslsBUJiycH5-Sx9JZOKjyerGDg?e=6daIID

Prescribing PEP

- In case of queries contact GU clinic or infectious disease specialists through MDH switchboard

- Both EACS and CDC guidelines recommend dolutegravir as one of the antiretroviral drug options for PEP in women who are trying to conceive and throughout pregnancy. This should however be accompanied by appropriate counselling to allow joint decision-making between patients and providers in view of the small non-statistically significant increase in neural tube defects

- Accurate drug history should be taken before PEP is prescribed, including the use of over-the-counter medication, vitamins/minerals, herbal remedies and recreational drugs

- There are numerous interactions with these medications. Always check for drug interactions e.g., with calcium supplements, iron supplements, multivitamins and antacids. Liaise with HIV pharmacist or contact Mater Dei Hospital Pharmacy (extension 6514, 6569). Liverpool Drug Interaction website is also very useful and readily available online on http://www.hiv-druginteractions.org

- Always discuss potential side-effects of PEP during initial consultation (refer to respective summary of product characteristics (SPC))

- In exceptional circumstances such as in patients with renal impairment or drug allergy, these cases should be discussed with ID/GU specialists accordingly

How to use PEP

Assessment and initial management

- Initiate PEP as soon as possible after exposure, preferably **within 24 hours,** but can be considered up to 72 hours (PEP is not recommended beyond 72 hours).

- An emergency three-day supply of PEP for early administration of treatment is available at Floriana Health Centre and GGH. This is for administration when access is restricted because of public holidays or weekends.

- **Duration of PEP should be 28 days**.

- In the event of a further high-risk sexual exposure in the last two days of the PEP course, the PEP should be **continued for 48 hours after the last high-risk exposure**.

- **Baseline investigations** prior to initiation of PEP should include:

    - ✓ *Renal profile*
    - ✓ *Liver profile*
    - ✓ *4th generation HIV test, hepatitis B surface antigen, surface antibody and core antibody (only if not known to be vaccinated with documented HepBsAb >10 IU, hepatitis C*
    - ✓ *Pregnancy testing in women considering PEP*
    - ✓ *Sexually transmitted infections (STIs) including syphilis, chlamydia, gonorrhoea following sexual exposure (to be done at first appointment at GU clinic)*

Monitoring and Follow-up

- **Routine blood test monitoring** after initiation of PEP is **only indicated** if:
    - ✓ Significant abnormalities are detected on baseline testing
    - ✓ New symptoms develop on PEP (e.g., rash, jaundice, muscle pain)
    - ✓ Recipient is pregnant
    - ✓ There is a risk of drug-drug interaction
    - ✓ Advisory, not mandatory
    - ✓ Significant comorbidities such as hepatitis or renal dysfunction exist

- **Early follow-up with GU/HIV clinician as applicable** for:
    - ✓ Repeat STI testing 2 weeks post-exposure
    - ✓ Repeat HIV, hepatitis C testing (and hepatitis B surface antigen if not immune) at 12 weeks after exposure
    - ✓ Follow up testing for hepatitis B should be guided by hepatitis B vaccination status and baseline immunity
    - ✓ Future sexual health check-ups at GU clinic

- Individuals experiencing a skin rash or flu-like illness during or after taking PEP should be advised to attend for urgent review to exclude an HIV seroconversion illness
- If the baseline HIV test is positive after PEP has already been initiated, continue PEP pending review by an HIV specialist

- Offer an ultra-rapid course of Hepatitis B vaccination if clinically indicated and the individual has no immunity at baseline

- Individuals missing doses of PEP should be counselled according to the:
    - ✓ Number of missed doses
    - ✓ Time elapsed from the last administered dose (see Table 3)

Scenario	Recommendation	Comments
< 24 hours elapsed since last dose	Take missed doses immediately and subsequent doses at usual time	Reinforce importance of adherence and re-evaluate motivation to continue PEP
24-48 hours elapsed since last dose	Continue PEP	Reinforce importance of adherence and re-evaluate motivation to continue PEP
>48 hours since last dose	Recommend stop PEP	

Table 2 Guidance of Missed doses of PEP

These guidelines are issued by the Office of the Chief Medical Officer and have been adapted with permission for use in the community setting from Mater Dei Hospital Clinical Guidelines.