HIV Post Exposure Prophylaxis (PEP) for those working internationally

Introduction

These guidelines apply to staff working or travelling internationally, who are involved in Exposure Prone Procedures, or who are considered to have other significant risks of exposure to Human Immunodeficiency Virus (HIV) infection because of their location or situation.

More people are travelling and working internationally than ever before, and HIV continues to spread in most countries. The estimated number of people living with HIV in 2014 was 36.9 million according to the World Health Organization (WHO). This means the risk of exposure to HIV infection is a continuing cause for concern. Risk is probably highest for health workers and those carrying out Exposure Prone Procedures, but other travellers can also be exposed. This is mainly from unprotected sex, including sexual assault, and after the use of unclean injection needles or other invasive health care equipment such as intravenous infusions and in dentistry.

Post-exposure prophylaxis (PEP) is the treatment taken as soon as possible after an at-risk incident. It reduces the risk of subsequently becoming HIV positive by about two thirds. InterHealth recommends that each organisation responsible for staff working internationally should seriously consider the option of making a 3 or 7 day PEP starter kit available for all health care staff or others carrying out Exposure Prone Procedures and possibly for other staff deemed at significant risk of exposure.

Because PEP needs to be started without delay, this means that kits should be taken by each individual health care worker or traveller deemed at risk, unless an immediate, reliable and always accessible source is available in the institution where they are working. The idea is that this initial 3-7 day kit should be with the staff member at all times, ready to start if needed. But then further PEP medication would need to be available to continue the full course for 28 days.

It is also important to remember the risk of other blood-borne diseases after incidents which might spread HIV. The most important is hepatitis B which is estimated to be many times more infectious than HIV. For this reason, all staff working or travelling internationally should have completed a full course of hepatitis B injections (3 or 4), and, in addition, any person involved in Exposure Prone Procedures should have their hepatitis B blood levels checked to ensure the course of injections has been effective. Hepatitis C is a smaller risk, for which there is no immunisation at present.

Sexual assault carries a high risk of a range of sexually transmitted infections and an early, thorough examination at a specialised Genito-Urinary Medicine (GUM or STI) clinic is essential as part of the follow-up procedures for any traveller who has been at risk. Sexual assault can happen to men as well as women and psychological support in the immediate aftermath is vital alongside physical tests and medications. Please be aware that InterHealth Worldwide also stocks a ‘Sexual
Assault’ kit which comprises of the PEP kit and other medications, supplies and advice, and may be more suitable for your needs. Please discuss this with one of our clinicians.

All those taking PEP with them must be thoroughly familiar with relevant policies of the organisation to which they belong, as well as being informed about availability, dosages and side-effects of PEP and the steps to be taken in case of exposure. Only in this context will it be possible for travellers to decide when to start PEP and to ensure that this is begun as soon as possible after exposure, ideally within one hour. This means, in addition, that staff must have made a provisional decision as to whether and when, in practice, they would use PEP if faced with a situation where there was a significant risk of exposure to HIV.

PEP should be started as soon as possible after exposure, preferably within 24 hours, but can be started up to 72 hours. PEP started within one to two hours after a high-risk incident, is thought to reduce the risk of subsequently becoming HIV positive from approximately 3 per 1000 to less than 1 per 1000.

**Incidents carrying a risk of HIV Infection**

1. **Health Care Workers and others carrying out Exposure Prone Procedures.**

These have a significant risk. The type of injury should be carefully assessed and graded as follows:

- **High:** an injury which penetrates the skin with a high-calibre, hollow-bore needle, visibly contaminated with blood, or from a needle that has been within an artery or vein of a patient, or any deep wound to the health care worker. Percutaneous or mucus membrane exposure to laboratory material or research specimens containing HIV; potentially infected blood transfusions.

- **Moderate:** any wound to the health care worker that bleeds and may be contaminated with blood or infectious body fluid*, e.g. a cut or needle-stick injury penetrating gloves: contact with mucous membranes or eyes, including from mouth-to-mouth resuscitation.

- **Low:** superficial wounds that do not bleed, any contact from body fluids considered to be non-infectious. Contact of any body fluid solely onto intact skin.

*Blood is the most infectious body fluid, followed by cerebrospinal fluid. Semen, vaginal secretions, synovial, pleural, peritoneal, pericardial, and amniotic fluid and breast milk also carry risk: all these are considered as infectious body fluids. The following are considered low-risk unless visibly blood-stained: urine, vomitus, saliva, faeces, tears, nasal secretions, sweat and sputum.

2. **Those exposed to HIV infection through other means**

There is a significant risk of exposure in the case of rape (female or male), depending on the exact circumstances. Normally an on-the-spot assessment needs to be taken as to the likely HIV status of the assailant. This is always difficult, but the categories listed under Step 2 below would increase the likelihood of infection. If in doubt, it is better to play safe and start PEP.
Penetrative sexual intercourse, vaginal, anal and occasionally oral, can lead to HIV. The presence of infected seminal fluid on any mucous membrane especially the vagina and anus but also others including the mouth should be considered an at-risk incident.

Other situations where PEP should be considered include a road or other accident with a penetrating injury involving blood, potentially or actually contaminated with HIV. HIV-infected blood coming into contact with either broken or chapped skin (including eczema), might also give rise to transmission of the virus. All blood should be treated with respect - it is not possible to judge if it is, or is not infected with HIV unless laboratory testing is available. However, unbroken skin is a good barrier against transmission of the virus.

Rarer situations which may cause HIV transmission include blood transfusions from an unknown or untested source, mouth-to-mouth resuscitation on individuals deemed to have a significant risk of being HIV positive, and spillage of blood on the broken skin or mucous membrane of an individual involved in an accident or other incident.

**Recommended procedure after a risk-prone incident**

These recommendations apply to occupational health incidents and to other situations as mentioned above.

In the case of a health worker with an occupational exposure the steps to be followed should ideally be supervised by a trained and designated person, usually the most senior medical officer, health care worker or manager available.

However in many settings this will not be possible and initiation of PEP should not be delayed for this reason. In this case the individual will have to decide whether or not to start self-treatment. If a suitable doctor is not available locally then you can contact the doctors at InterHealth remotely for advice. As soon as possible the individual should place themselves under the supervision of an experienced medical colleague, and reconsider after 72 hours whether there is an evidence-based or perceived need to complete the full 28 day course. Unless there is a clear reason to discontinue, the full 28 days should be completed.

**Step 1: Immediate Action**

In the case of an injury allow the wound to bleed, if necessary helping with gentle pressure, but do not squeeze. Wash the wound and surrounding area with soap and water. If the eyes are affected, rinse carefully with water or sterile saline for 10 minutes. If the mouth is affected, rinse thoroughly with water or saline.

**Step 2: Assess severity of exposure or injury**

This step applies mainly to health care workers in occupational settings. Any assessment needs to be made by the most experienced senior health care worker available. It is a matter of a careful risk assessment. The descriptions given are guidelines only as there is insufficient evidence to offer more precise definitions.

Two factors need to be assessed:
Magnitude of exposure: See under ‘Health care workers carrying out Exposure Prone Procedures’ above.

Source patient: Categorized as either a significant risk of HIV infection OR source patient probably not infected with HIV.

Sometimes the source patient will be known to be, or considered likely to be HIV positive. More commonly an estimate will need to be made. Several criteria can be used for this.

These include:

- Known high-risk sexual activities
- Suggestive symptoms or signs of AIDS or HIV-associated illnesses
- High local prevalence rates of HIV

The possibility of determining the HIV status of the source patient should be discussed with a senior colleague.

Step 3: Follow the wishes of the individual who has been exposed

Each individual is strongly encouraged to make a prior decision as to whether they wish to start PEP in the case of an at-risk injury or other accidental exposure.

Step 4: Use PEP where indicated

Use this table below as a guide for health care workers:

<table>
<thead>
<tr>
<th>Magnitude of Exposure</th>
<th>Source patient: possibly high risk</th>
<th>Source patient: probably low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>PEP Recommended</td>
<td>Consider PEP</td>
</tr>
<tr>
<td>Moderate</td>
<td>PEP Recommended</td>
<td>Consider PEP</td>
</tr>
<tr>
<td>Low</td>
<td>PEP not necessary</td>
<td>PEP Not Necessary</td>
</tr>
</tbody>
</table>

Current recommendations are that once started, PEP should be continued for 28 days under the care of a suitable medical practitioner and with appropriate monitoring.

From 2014, The Expert Advisory Group on AIDS in the UK recommends that the preferred first-line regimen for PEP (for occupational and non-occupational use) is Raltegravir and Truvada for 28 days. A brand name of Raltegravir is Isentress, and Truvada is comprised of 245mg tenofovir disoproxil (as fumarate) and 200mg emtricitabine (FTC). Raltegravir is an HIV-integrase inhibitor and Truvada is a nucleoside reverse transcriptase inhibitor (NRTI).

Previously standard guidelines on the use of PEP in health care settings in the UK have recommended the use of a combined preparation of Zidovudine and Lamivudine (previously known as Combivir), along with Kaletra which comprises two separate drugs (lopinavir and ritonavir). Zidovudine and Lamivudine belong to a class of drugs known as NRTIs, and Kaletra to a class of...
known as Protease Inhibitors. Kaletra and Truvada together is another combination previously recommended. The use of Combivir on its own is no longer recommended.

The reasons for the recommendation of Raltegravir/Truvada are that there are no significant safety issues with this combination from extensive testing in HIV-infected patients and Raltegravir is better tolerated than Kaletra, so switching is likely to improve adherence, and hence efficacy, of PEP.

The side-effects of Kaletra are common and troublesome, making it less likely that treatment will be completed. In one study between 17% and 40% of those starting protease-containing PEP, such as Kaletra, failed to complete the 28-day course because of side-effects.

The Raltegravir/Truvada combination is more expensive. Completion courses, after the starter packs of Raltegravir/Truvada, can sometimes be more difficult to source in resource-poor countries.

All options available are considered effective and if a starter course is commenced and these drugs are not available to complete the course, you can switch to the best available alternative.

At InterHealth we are able to provide Raltegravir with Truvada or Zidovudine/Lamivudine (generic Combivir) with Kaletra. PEP is expensive. In practice, each individual or organisation will need to make their own choice based on cost and the perceived risk of course completion due to tolerability.

**Recommended dosages**

1. **Zidovudine/ Lamivudine (generic Combivir) and Kaletra**

   Zidovudine 300mg/ Lamivudine 150mg tablets should be taken at a dose of one tablet twice daily for 28 days.

   Kaletra film-coated tablets should be taken at a dose of two tablets twice daily for 28 days. Each tablet consists of lopinavir 200mg and ritonavir 50mg.

**Contraindications**

There are no absolute contraindications for Combivir which is also considered generally safe in the 2nd and 3rd trimesters of pregnancy. The addition of Kaletra adds to the risk of side effects and drug interactions. Kaletra is not advised in breastfeeding and is best avoided in pregnancy unless after a high-risk incident.

**Side effects**

For Combivir these are usually mild but they can include nausea, diarrhoea, muscle pain, rash and headache. Anaemia can sometimes occur. Kaletra may cause more troublesome side-effects including diarrhoea, nausea, abdominal pain, weakness and headache, also, sometimes, an increase in blood sugar making it less appropriate for diabetics. Side-effects can be reduced by adjusting the timing within a 24-hour period when drugs are taken. Individuals should find out what works best for them and use medicines to reduce the side effects such as cyclizine for nausea and loperamide for diarrhoea, if required.
Drug Interactions

Combivir: Trimethoprim, phenytoin, valproic acid, clarithromycin (may be taken if the doses are taken 2 hours apart from the Combivir), fluconazole, emtricitabine (in Truvada), non-steroidal anti-inflammatory drugs such as ibuprofen, diclofenac and naproxen.

Kaletra: Kaletra interacts with numerous drugs. Some of the interactions are with anti-epileptics, calcium-channel blockers (taken for high blood pressure), statins, Riamet (co-artemether) antidepressants, antipsychotics and contraceptives. Please check the Patient Information Leaflet for further interactions.

2. Raltegravir and Truvada

Raltegravir 400mg tablets should be taken at a dose of one tablet twice a day.

Truvada tablets should be taken at a dose of one tablet once a day. Truvada consists of tenofovir disoproxil 245mg (as fumarate) and emtricitabine 200mg.

Contraindications

Raltegravir should be avoided in pregnancy and breastfeeding. Truvada can be used in pregnancy but not whilst breastfeeding.

Side-effects

Raltegravir is generally well tolerated but its side-effects can include decreased appetite, abnormal dreams, insomnia, nightmares, abnormal behaviour, depression, abdominal distention, abdominal pain, diarrhoea, flatulence, nausea, vomiting, and dyspepsia. Side-effects of Truvada include headache, dizziness, nausea, diarrhoea, insomnia, abnormal dreams, abdominal pain, abdominal distension, flatulence and rash.

Drug Interactions

Raltegravir: Antacids, rifampicin, darunavir, orlistat, famotidine and omeprazole.

Truvada: Lamivudine (in Combivir), orlistat, adefovir, atazanavir, didanosine, lopinavir, telaprevir, orlistat.

These lists are by no means exhaustive. Please read the Patient Information Leaflets before taking these medicines and check with a healthcare professional that they are suitable for you BEFORE you may have to take them. Those who start PEP should be strongly advised to continue for 28 days, as side-effects usually become less with time.

Step 5: Follow up

The following tests are recommended as a baseline:

1. **At or shortly after the incident:** HIV, HCV, & HBV whether or not PEP is being taken.

2. **If PEP is started:** FBC and liver tests are recommended, in addition, to check that your body is coping with being on the PEP medication.
3. **Follow up:** Follow up should be under the care of a specialist, following national guidelines e.g. [http://www.bashh.org/documents/PEPSE%202015%20guideline%20final_NICE.pdf](http://www.bashh.org/documents/PEPSE%202015%20guideline%20final_NICE.pdf)

<table>
<thead>
<tr>
<th>Timing</th>
<th>In Persons Taking PEP</th>
<th>In those Not Taking PEP</th>
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<tbody>
<tr>
<td>At or shortly after incident</td>
<td>HIV, HCV, HBV, FBC &amp; liver transaminases</td>
<td>Baseline HIV, HCV, HBV ideally within 8 days of exposure</td>
</tr>
<tr>
<td>Week 4</td>
<td>Transaminases, FBC, (BS),(Amylase)</td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td>HIV,HCV, HBV &amp; transaminases</td>
<td></td>
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<tr>
<td>Month 6</td>
<td>HIV, HCV, HBV&amp; transaminases</td>
<td>Month 6 HIV, HCV, HBV&amp; transaminases</td>
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</tbody>
</table>

- HCV stands for hepatitis C antibodies
- HBV stands for hepatitis B antigen and antibodies
- FBC stands for full blood count which includes levels of red cells, white cells, platelets and haemoglobin
- Transaminases are indicators of liver function
- BS refers to blood sugar measurement for those taking protease inhibitors which should ideally also be done at week 2
- Amylase is only needed for those taking Kaletra

The purpose of testing for transaminases is largely to detect any signs of hepatitis, and to make sure that Kaletra, in particular, is not affecting the liver.

If the source patient has a high perceived risk or known infection with hepatitis C, a viral RNA test should be done approximately 6 weeks after exposure.

Those who have confirmed protective levels of immunity against hepatitis B do not need to have HBV tests.

In addition:

- In the case of a health care setting, an incident form needs to be completed by the senior health worker in charge.
- Regular clinical assessment should be made both for signs of a primary infection within the first 3 to 6 weeks, and for monitoring side-effects of any treatment. Primary infection is the cluster of symptoms when a person is in the process of becoming HIV positive i.e. is sero-converting. The most common symptoms to watch for are rash and ‘flu-like’ symptoms but most people who are infected with HIV do not experience a sero-conversion illness.
- Counselling and support must be offered to the healthcare worker, or individual exposed for whatever reason until known to be HIV negative or to have sero-converted. Frequently those exposed are distressed after an incident, sometimes after a time-delay, and in addition to being counselled in person may also wish to speak or have an email consultation with an

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expert from their home country. InterHealth Doctors and Psychological Health clinicians can
be available for remote support either by telephone or email.

- Medical personnel should be mindful that if the exposure situation involves sexual assault
  rather than an occupational exposure then it may not be appropriate to discuss this with your
  colleagues. Therefore you should research in advance where you can go for psychological
  support and medical tests.

Step 6: Decide on the best location for the person exposed

In the case of health care workers there are various options to be considered if PEP is being used:

- Remaining on-site. Many people, especially longer term health workers and aid workers may
  opt for this but certain minimum requirements must be in place (see below).

- Moving to a regional centre where follow-up can be supervised by a specialist.

- Repatriation to the healthcare worker’s home country.

- Medical and nursing elective students would normally be advised to return home.

- Each agency will need to decide which is most appropriate for their own circumstances. Many
  agencies have clear, non-negotiable guidelines on this issue.

For the client to remain on-site the following will need to be in place:

- The presence of effective support and counselling.

- The freedom to be able to discontinue work when under treatment, if side-effects make this
  necessary.

- Competent medical supervision from a well-informed doctor either based on-site or within
  reasonable distance.

- Access to reliable laboratory testing for tests mentioned above. It is sometimes possible to
  send certain samples to a reliable laboratory in the capital or back to the country of origin.

- The express wish of the client to remain on site, rather than to be repatriated.

- The absence of any serious side-effects from the treatment, other significant illness or any
  suggestion of a primary infection.

Those exposed to HIV who require PEP should be followed up in an environment where testing,
monitoring and provision of PEP is available. Clients who have experienced a high-risk incident,
whether or not taking PEP, should seek advice from their occupational health department about
whether they should continue any medical work until they have received a definitive negative HIV
test result. They should, however, ensure that sex is fully protected, should avoid becoming
pregnant, and must not breast-feed until they have received a definitive negative HIV test result.

In the case of those sexually assaulted, medical evacuation to a place of safety is advisable so
that appropriate support, counselling and medical care is available. This will usually either be a
regional centre or the individual’s country of origin. It is a decision which should normally be made primarily by the person involved, but with appropriate advice and support from any colleagues whom they may wish to inform.

PEP is prescribed for an individual after consultation with a specially trained nurse or doctor and should not be passed on to others.

**Logistics of PEP supply**

Best practice is increasingly being seen as having PEP available for immediate use by those with a significant occupational health risk. This means that each individual should be given the option of taking their own personal supply. In health care settings, in addition or as an alternative, supplies can be held in the institution where they are working, under the responsibility of a designated person, ideally the most senior health worker present. However, procedures must be in place so that this supply is readily available at all times.

**Medical electives or UK healthcare workers posted on short-term assignments from the NHS**

Will be advised to follow the latest UK guidelines and will therefore be required to take Raltegravir and Truvada.

**Prior to departure**

A 3 day starter pack of Raltegravir and Truvada or 3-day, 5-day or 7-day starter packs of Zidovudine/Lamivudine (generic Combivir) and Kaletra can be issued. There must be a plan in place to provide supplies to continue to provide PEP drugs without interruption for the full 28-day period. This may be at the location of the assignment, in a regional centre, in another country or in the home country.

**Storage and shelf life**

Drugs should be stored in a dry, dark place ideally between 2°C and 30°C. Expiry dates must be regularly checked.

**Security**

If it is known that valuable, restricted-use, potentially life-saving drugs are being kept on the premises, there may be significant risks of robbery or intimidation. Those entitled to use PEP must know how and where to access supplies through a 24-hour period.

**Further supplies**

Further PEP supplies to complete the 28-day course, for those who remain on site, must be reliably available either on-site or through regional depots, under the control of either the employing organisation, or an inter-agency co-ordinating group.

**On return from a mission or assignment**

Staff members must check the expiry date. If this has passed, the PEP should be taken to a pharmacist for safe disposal. If it remains within the expiry date it could be used on a further
mission or period of travel, provided it has been stored correctly. PEP should not be passed on to a friend or colleague. It cannot be returned to the supplier.

**Ethical Considerations**

InterHealth recommends that organisations as Equal Opportunities employers who adhere to and support a non-discriminatory HIV policy, should consider making PEP available to all those working internationally who are involved in Exposure Prone Procedures, regardless of country of origin and to all nationally recruited staff working in a health care setting with a significant occupational health risk.

**Conditions of supply**

**Supply in the UK**

Before InterHealth can dispense PEP, a trained travel health nurse must have a consultation either in person or by pre-arranged phone call lasting approximately 15 minutes, with the person buying the kit to ensure they fully understand the indications and conditions of its use. There is a small charge for this consultation. Each individual also needs to complete a simple form.

**Supply in Nairobi**

Please contact the Nairobi office for details.

**Supply in other countries**

For many staff members recruited outside the UK it will be more appropriate to obtain supplies within country or region. However appropriate safeguards, modelled on the InterHealth conditions of supply, should be followed.

**Further Guidance and Information**

- HIV Post-Exposure Prophylaxis: Guidance from the UK Chief Medical Officers
- UK Guideline for the use of HIV Post-Exposure Prophylaxis Following Sexual Exposure (PEPSE) 2015 - BASHH
- Website to check for drug interactions with HIV medications: [http://www.hiv-druginteractions.org/](http://www.hiv-druginteractions.org/)
Please note none of these documents refer specifically to the use of PEP in travel-related contexts.

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