Guidelines for non-occupational post-exposure prophylaxis (nPEP) following exposure to body fluids

The Australasian Society for Infectious Diseases (ASID)
Australian and New Zealand Paediatric Infectious Diseases Group

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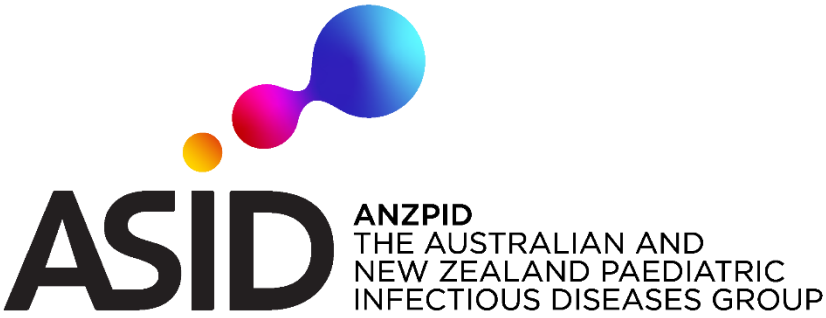

Who does this guideline apply to?

- This guideline represents a stepwise approach for managing children at risk of blood-borne infections and where relevant, sexually transmitted infections, following non-occupational exposure to body-fluids. This includes children following sexual assault, human bites and splash injuries.
- nPEP is generally not required for community-acquired needle stick injuries and for further information on community-acquired needle stick injuries please refer to local guidelines.

Background

- In Australia, the seroprevalence of HIV is 0.1% (1); 90% of people living with HIV know their diagnosis, 96% are in care, of which 92% are receiving anti-retroviral therapy (ART), of whom 97% are **virally suppressed** (2).
- HIV prevalence is higher in men who have sex with men (MSM) population (10%), people who inject drugs (PWID; 1%), transgender populations (1.2%) (3) and is higher still for MSM individuals who also inject drugs (30%) (1).
- Undetectable viraemia ≥6 months in the source case protects against onward transmission (Undetectable = untransmissible or U=U) (4-7).
- Few randomised control trials of nPEP have been conducted (8). Recommendations are largely informed by data from animal studies, observational studies in humans (9-12), and expert opinion; this includes the collective experience of the ANZPID group in using anti-retroviral therapy in children with chronic HIV.
- Inappropriate administration of nPEP in cases where it is not required increases the risk of medication-related side-effects/adverse events, is costly, and can increase the stress experienced by an acutely traumatised child.

Recommended management

1. Consider whether forensic exam is indicated and if so, refer to your local child protection unit for a multidisciplinary assessment. Ensure a mandatory notification has been made, if required.

2. Assess the transmission risk for HIV and whether nPEP is warranted

Rsk of HIV transmission **= Risk of HIV viraemia in the source individual x exposure activity risk**

- Discussion with a paediatric HIV specialist/Infectious Diseases physician is recommended for all cases
- The risk of HIV viraemia in the source case can be extrapolated from the risk of HIV viraemia in the source population (13, 14).
- High risk groups are those where there is a significant likelihood of the index case individual being HIV-positive. High prevalence countries are defined as >1% HIV. HIV prevalence data by country can be found at https://aidsinfo.unaids.org
- See *Table 1* for approach to risk stratification:

Table 1 *Risk stratification and recommendations for nPEP*

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	INDEX HIV POSITIVE		INDEX UNKNOWN HIV STATUS	
	HIV VL unknown or detectable	**HIV VL undetectable**	**High-risk group (MSM, high prevalence country & no screening, PWID)**	**Low risk group**
SEXUAL EXPOSURES				
Receptive anal sex	Recommended	Not recommended[a]	Recommended	Not recommended
Insertive anal sex	Recommended	Not recommended[a]	Consider case by case[b]	Not recommended
Receptive vaginal sex	Recommended	Not recommended[a]	Not recommended	Not recommended
Insertive vaginal sex	Recommended	Not recommended[a]	Not recommended	Not recommended
Fellatio with ejaculation	Not recommended	Not recommended[a]	Not recommended	Not recommended
Fellatio without ejaculation	Not recommended	Not recommended[a]	Not recommended	Not recommended
Splash of semen into eye	Not recommended	Not recommended[a]	Not recommended	Not recommended
Cunnilingus	Not recommended	Not recommended[a]	Not recommended	Not recommended
Digital penetration	Not recommended	Not recommended[a]	Not recommended	Not recommended
OTHER EXPOSURES				
Sharing of injecting equipment	Recommended	Not recommended[a]	Generally not recommended	Not recommended
Sharps injury	Recommended	Not recommended[a]	Generally not recommended	Not recommended
Mucosal splash injury	Recommended	Not recommended[a]	Generally not recommended	Not recommended
Human bite	Not recommended	Not recommended[a]	Not recommended	Not recommended
Community acquired needlestick	Not recommended	Not recommended[a]	Not recommended	Not recommended
Recommend: the benefits of PEP are likely to outweigh the risks, PEP should be given unless there is a clear reason not to.				
Consider case by case: the risk/benefit balance of nPEP is less clear. The risk should be assessed on a case by case basis. Factors that influence decision-making are listed in footnote b.				
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 footnote b)				
Not recommended: the risk of HIV transmission is negligible and PEP should not be given.				
a: On ART >6 months with undetectable HIV VL throughout and good adherence.				
b: Factors that may increase the risk of HIV acquisition (and consideration of nPEP use) include: (1) The assault: confirmation of penetrative assault (and number of episodes), whether there is evidence of mucosal injury, whether ejaculation has occurred, the timing of the assault i.e. <24 hours, 24-72 hours versus >72 hours (2) The victim: the younger the child (pre-pubertal mucosa), the higher the risk (3) The perpetrator: whether there is confidence about other high-risk behaviours e.g. IVDU or MSM and (4) The context: whether follow-up will be achievable, the nature of the child's environment, whether compliance is likely to be achieved and the likelihood of drug interactions (5) Sexually transmitted infections in either person				

1. If nPEP is indicated, determine the regimen choice based on age and weight.

Table 2 Recommended nPEP regimen choice

Age	***PREFERRED REGIMEN (note must be >35kg)***
Children >6y	Truvada® (Emtricitabine with Tenofovir disoproxil fumarate) PLUS Dolutegravir* OR Raltegravir
	ALTERNATIVE >25kg
	Biktarvy® (Biktegravir + tenofovir alafenamide + emtricitabine)**
Children <6y or <25kg	***PREFERRED REGIMEN***
	Lamivudine + Zidovudine PLUS Dolutegravir* OR Raltegravir
	Note: Zidovudine and Lamivudine are also available as a combination product (Combivir ®) for patients
*When available, dolutegravir is preferred over raltegravir due to it's once daily dosing, smaller pill size and tolerability	
**Single fixed drug combination therapy with Biktarvy may be considered if this regimen is expected to improve compliance with	

2. Having decided on the nPEP regimen – prescribe according to Table 3 based on weight band and preferred formulation.

- Advise young person/family of potential side effects and how best to take the medicines.
- Availability of medicines and formulations may vary at different sites.

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Table 3 Medications and potential side-effects

Medication	Preparations	Dose	Potential side-effects	Administration
Biktarvy®	Bictegravir 50mg + tenofovir alafenamide 25mg + emtricitabine 200mg combination tablet (purplish-brown)	**≥6 years and >25kg:** 1 tablet daily	Nausea, diarrhoea, fatigue, headache, unusual dream, depression/suicidal ideation	DO NOT crush. Take with or without food. AVOID antacids/ multivitamins Tablet may be dispersed in 20mL of orange juice
Dolutegravir	50mg tablet (yellow)	**≥20kg:** 50mg daily	Insomnia, mood changes, headache, hepatitis, rash, weight gain	Take with food. AVOID antacids/ multivitamins. Tablet may be cut or crushed. Previous concerns regarding small increase in neural tube-defects in children born to pregnant women; not substantiated on meta-analysis
Truvada®	Tenofovir disoproxyl fumarate 245mg + emtricitabine 200mg combination tablet (blue)	**≥35kg:** 1 tablet daily	Headache, nausea/vomiting, abdominal pain, rash, loss of appetite, renal or hepatic impairment, bone problems	Take with food
Lamivudine	10mg/mL liquid	4mg/kg/dose BD	Nausea, diarrhoea, headache, fatigue	Take with/without food. Tablets can be crushed and mixed with food/water
	OR			
	150mg tablet (white)	**14-21kg:** 75mg BD **21-30kg:** 75mg AM, 150mg PM **≥30kg:** 150mg BD		
Zidovudine	10mg/mL liquid	180mg/m2/dose BD	Granulocytopenia, anaemia, nausea, headache, myopathy, hepatitis, nail pigmentation, neuropathy	Take with/without food. Capsules can be opened and contents dissolved in water
	OR			
	100mg or 250mg capsule (blue/white)	**18-14kg:** 100mg BD **15-23kg**: 100mg AM, 200mg PM **24-34kg:** 200mg BD **≥35kg:** 250mg BD		
Combivir®	Zidovudine 300mg + lamivudine 150mg combination tablet (white)	**14-21kg:** 1/2 tablet BD **21-30kg:** 1/2 tab AM, 1 tab PM **≥30kg:** 1 tablet BD	As per individual agents	Can be cut or crushed and taken with/without food
Raltegravir	**CHEWABLE TABLET*** 25mg (yellow) 100mg (orange/beige) *Chewable and standard tablets are **NOT** bioequivalent. Patients ≥25kg may use either weight-based dosing (chewable tablet) or adult dosing (standard tablet)	**CHEWABLE:** **<11kg:** 6mg/kg BD **11-14kg:** 75mg BD **14-20kg:** 100mg BD **20-25kg:** 150mg BD **25-28kg:** 150mg BD **28-40kg:** 200mg BD* **≥40kg:** 300mg BD*	Nausea, dizziness, insomnia, rash, pancreatitis, deranged liver function and creatine kinase	Tablets can be cut or crushed and taken with/without food. AVOID antacids/ multivitamins 4 hours before and after each dose
	OR			
	STANDARD TABLET* 400mg (pink)	**STANDARD**: **≥25kg and ≥ 6years**: 400mg BD		

3. Consider which investigations should be performed.

Table 4 Recommended investigations for children following non-occupational exposures to blood-borne infections.

Test	Baseline	4-6 weeks	3 months
HIV serology	X		X
Hepatitis B serology[a]	X		X
Hepatitis C serology[b]	X		X
Syphilis serology[c]	X		X
Gonorrhoea & chlamydia urine PCR[c]	X	X[d]	
FBC/UEC/LFT[e]	X		
Pregnancy test	X	Consider repeating if indicated	
[a]Regardless of vaccination status			
[b]Hep C RNA PCR may be considered as a preferable screening test if high-risk exposure			
[c]If following sexual assault +/- pharyngeal/anal swabs as appropriate			
[d]If not treated presumptively at baseline, or if symptomatic			
[e]For children commenced on nPEP, electrolytes (UEC) and liver function (LFT) testing recommended; Full blood count (FBC) suggested if child is commenced on zidovudine			

4. Determine whether there is protection against hepatitis B

If baseline anti-HepBsAb is not protective (<10iU/L), administer the following (ideally within 72 hours of the exposure incident but up to 10 days is permissible):

Hepatitis B vaccination (Engerix B® Paediatric; 10 microgram, 0.5mL IM)
AND
Hepatitis B immunoglobulin 100 units IM if <30kg and 400 units if >30kg

5. If penetrative sexual assault, consider empiric antibiotics.

If testing in a timely manner and/or follow up is not guaranteed, the following empiric treatment is recommended to protect against chlamydia, and gonorrhoea, respectively:

Azithromycin: 20mg/kg (maximum 1g) PO STAT
AND
Ceftriaxone: 50mg/kg (maximum 500mg/dose) IV/IM STAT

6. For young people at ongoing risk of HIV acquisition (e.g. consensual sex with serodiscordant couple), consider whether PREP is indicated in accordance with the ASHM guidelines.

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