PEP-in-Pocket (PIP)

Provider Toolkit

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Note that the information contained within this document is subject to change as guidelines and best practices are updated.

Overview

HIV Post-Exposure Prophylaxis-in-Pocket (PEP-in-Pocket or "PIP") is a proactive strategy aimed at preventing HIV transmission among individuals who experience infrequent exposures to HIV (e.g., 0-4 per year) that are often (but not always) unanticipated. PIP involves prescribing a *complete* 28-day course of guideline-approved HIV Post-Exposure Prophylaxis (PEP) antiretroviral (ARV) medications and providing detailed instruction on their usage. Patients are advised to fill their prescription and store the medication in a secure and accessible location. They are instructed to self-initiate ARVs as soon as possible, and within a 72-hour window for any potential HIV exposure, and then follow up with their PIP provider on a less urgent basis, typically within 7-10 days of ARV initiation.

Providing patients with the full 28-day course of ARVs plays a critical role in overcoming the significant barriers to accessing PEP care.

PIP should be included as part of the provision of comprehensive HIV prevention services that includes regular evaluation of HIV risk, adherence counselling, HIV education and risk reduction counselling.

In summary, PIP involves:

- Identifying people who experience 0-4 HIV exposures (often unanticipated) per year.
- Providing a 28-day prescription for guideline-approved PEP ARVs.
- Supporting people filling this prescription.
- Education on how and when to initiate medications.
- Instructions to follow up in clinic after initiating ARVs and/or at regular 5-6 month intervals for testing and routine laboratory investigations.

Who Should Be Offered PIP?

PIP may be a suitable option for individuals of any sex/gender who are concerned about their risk of HIV infection and experience 0-4 exposures per year. Some individuals opt for PIP after having to seek PEP initially; some who initially seek PrEP decide PIP is a more suitable option based on their current risk. **Many individuals switch between PIP and PrEP based on their evolving and dynamic HIV risk and personal preference.**

Examples of individuals who may benefit from PIP include:

- Those at risk for HIV but prefer not to take PrEP.
- Those taking on-demand PrEP (also known as event-driven or 2-1-1 PrEP) who are not always able to anticipate a potential exposure or are not adherent to their medications.
- Those who have stopped taking PrEP and would like to have PIP as a safety net.
- Sex workers who are able to use condoms the majority of the time, but who may encounter challenges negotiating condom use.
- Anyone who has experienced a condom slip or break.
- Individuals who occasionally engage in unplanned condomless sex with partners of higher or unknown HIV risk.
- People who use injection drugs and may infrequently share equipment.
- Anyone who has sought PEP within the last 6 months.

Why PIP?

HIV PIP:

- Harnesses the well-established high efficacy of guideline-approved PEP for HIV prevention.
- Empowers patients with autonomy and control over their HIV prevention care.
- Enables immediate access to ARVs and avoids time-consuming visits to emergency departments or urgent care centers following an exposure.
- Eliminates most barriers associated with obtaining PEP through current methods.
- Mitigates the lack of evidence for on-demand PrEP in those with very infrequent HIV exposures.
- Bridges the gap in HIV preventative care between PEP and PrEP.
- Reduces costs and pill burden for individuals with a low frequency of exposures.

Cost of PIP in Ontario

In Ontario, **coverage is available** for most individuals. A knowledgeable provider, pharmacist or social worker can help navigate program applications.

- OHIP Plus (+) - 100% covered for those under the age of 25.
- Interim Federal Health (IFH) - 100% covered.
- Ontario Works (OW) - 100% covered.
- Ontario Disability Support Program (ODSP) - 100% covered.
- Private Insurance—coverage varies by plan.
- Trillium Drug Program—coverage depends on income and frequency of program use.

Canadian PEP Guidelines

Canadian guidelines[1] for prescribing PrEP and PEP were published in 2017 and updated in 2018. These guidelines can be found here: CMAJ Guidelines for PrEP and PEP

Canadian guidelines[1] are currently being updated and will include guidance on the prescription of PEP-in-Pocket for HIV prevention.

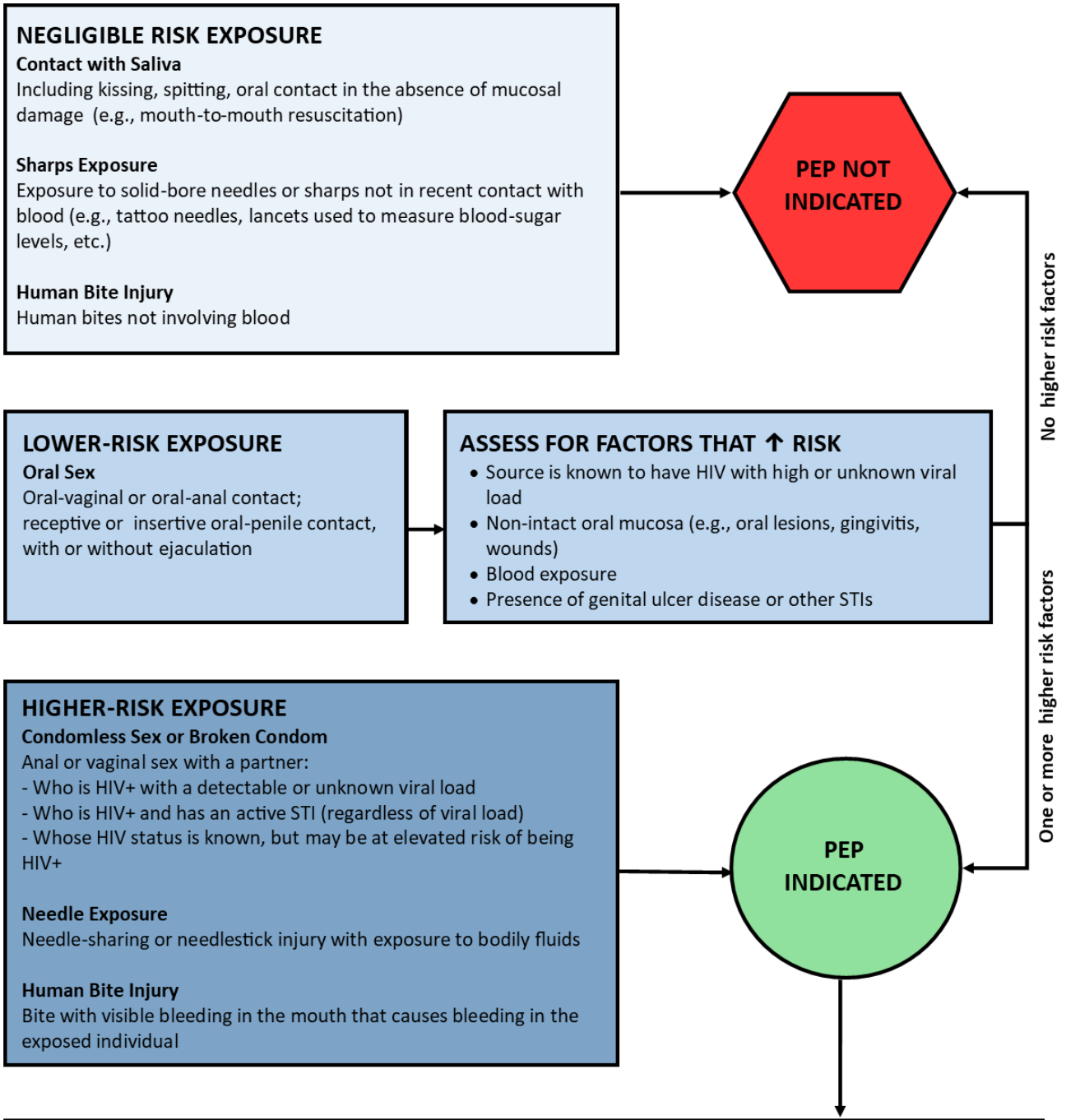
Risk Assessment

ARVs are most effective if initiated as soon as possible (e.g. within two hours) and not more than 72 hours after a potential HIV exposure. Individuals using PIP for HIV prevention should receive adequate education around risk assessment, and what is considered a potential exposure to HIV.

The following should be considered as part of a risk assessment:

1. Source person(s), if available.
2. Exposed person.
3. The nature of the exposure, including any factors that increase the risk of HIV transmission.

FIGURE 1: RISK ASSESSMENT FOR PEP/PIP INITIATION



	PREFERRED REGIMEN	ALTERNATE REGIMEN(S)
AGE 16+ OTHERWISE HEALTHY	BIC/FTC/TAF 50/200/25mg) QD	TDF/FTC (300/200mg) QD + DTG (50mg) QD or TDF/FTC (300/200mg) QD + RAL (400mg) BID
PREGNANT, OR POSSIBLY PREGNANT	TDF/FTC (300/200mg) QD + DTG (50mg) QD	TDF/FTC (300/200mg) QD + RAL (400mg) BID

Who Can Prescribe PIP?

Any licensed healthcare professionals who can prescribe medications are able to prescribe ARVs. Specialization in infectious diseases or HIV medicine is not required.

Recommended Drug Regimens

PIP/PEP is a 28-day course of a 3-drug ARV combination. Since adherence is critical for efficacy, it is advisable to opt for regimens that minimize side effects, number of doses per day and the quantity of pills per dose. As PEP guidelines differ in various regions, we recommend that PIP prescriptions adhere to local PEP guidelines. Below are the suggested PIP regimens used in Ontario.

TABLE 1: RECOMMENDED DRUG REGIMENS FOR PEP-IN-POCKET

	Preferred Regimen	Alternative Regimen(s)
Otherwise healthy adults and 16+ adolescents	B/FTC/TAF (50/200/25mg) once daily	TDF/FTC (300/200mg) once daily + DTG (50mg) once daily OR TDF/FTC (300/200mg) once daily + RAL (400mg) twice daily
Pregnant, or possibly pregnant	TDF/FTC (300/200mg) once daily + DTG (50mg) once daily	TDF/FTC (300/200mg) once daily + RAL (400mg) twice daily

B/FTC/TAF = bictegravir/ emtricitabine/ tenofovir alafenamide (Biktarvy®)
TDF/FTC = tenofovir disoproxil fumarate/ emtricitabine (Truvada®)
DTG = dolutegravir (Tivicay®)
RAL = raltegravir (Isentress®)

Drug Interactions

Taking ARVs alongside antibiotics, hormonal contraceptives, gender-affirming hormone therapy, methadone, and most over-the-counter drugs is generally safe. However, certain medications and supplements may impede the absorption of some ARVs, diminishing their effectiveness. To mitigate this risk, ARVs should be consumed at least 2 hours before or 6 hours after taking:

- Mineral supplements (such as calcium, iron, or magnesium)
- Antacids (such as Tums or Maalox)
- Laxatives
- Sucralfate

Drug interactions for specific ARV regimens can be assessed using the HIV/HCV Drug Therapy Guide | UHN (hivclinic.ca)

Adherence to Medications

Patients should be advised to take their medication at approximately the same time daily and informed that missing doses could reduce the drug's effectiveness. If a dose is forgotten, patients **should not take a double dose,** but rather take it as soon as remembered and resume their regular schedule thereafter.

Side Effects of Medications

Side effects of these medication are rare, but may include nausea, diarrhea, headache, fatigue, and insomnia. These symptoms are usually mild and tend to resolve within the initial days of treatment. Taking the medication with food may help alleviate nausea.

Less common, but more serious side effects may include kidney problems and muscle pain or weakness, however these are typically associated with prolonged use of ARVs.

Patients should be encouraged to adhere to their medication as prescribed, even if they are experiencing side effects. However, they should consult with their PIP provider as soon as possible should they develop side effects to discuss the appropriateness of changing or discontinuing medications.

Baseline Assessment

Baseline assessment for PIP is consistent with the baseline assessment for PrEP. Details can be found in Table 3, as well as the Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational post-exposure prophylaxis.[1]

Laboratory Investigations

Routine laboratory evaluations and screening for STIs, creatinine, HIV* and HCV testing, syphilis serology, chlamydia and gonorrhea (GC/CT) screening (oropharynx, rectum, urine), and pregnancy testing, if appropriate. All patients should have a serum creatinine performed at baseline to ensure that their eGFR is >60ml/min.

If acute HIV infection is suspected, additional laboratory evaluation with an HIV RNA nucleic acid amplification test (if available) or repeat fourth-generation assay 7 to 21 days later is suggested. PEP/PIP should not be withheld pending the results of these investigations. If the exposed individual is subsequently found to be HIV positive and has started on PEP, the antiretroviral regimen should be continued, and an HIV expert should be consulted as soon as possible.

Clinical Evaluation

Patients should be evaluated for symptoms of HIV seroconversion and counselled on HIV risk, including appropriateness of PIP versus PrEP strategies. HIV prevention modalities (e.g. PIP or PrEP) may be changed based on patients' current HIV risk, projected HIV risk, and patient preference. Adherence counselling and HIV education should be performed, as well as enquiring about mental health issues, alcohol, or drug use and abuse, and linking to appropriate care.

*We recommend that baseline testing be conducted with a lab-based fourth-generation HIV test.

Provision of PIP Prescription

Patients can be provided with a prescription for ARVs as per the guidance above. If needed, patients should be supported in obtaining their prescription at minimal out-of-pocket expense. Patients should also be counselled to store their medication in a secure and readily accessible location, which ensures immediate access in case of potential HIV exposure.

Guidance on PIP Usage & Adherence

TABLE 2: GUIDANCE FOR PATIENTS USING PIP

1	WAS YOUR POTENTIAL EXPOSURE HIGH RISK? Did you have condomless anal, vaginal/front hole sex, or have a condom slip or break during sex with a partner: · Who is HIV+ and has a detectable or unknown viral load? · Who is HIV+ and has an active STI? · Whose HIV status is unknown, but may be at elevated risk of being HIV+? Did you share any injection drug equipment?
2	IF YES, START TAKING YOUR PIP If you answered yes to any of the questions above, start taking your medication as soon as possible and within 72-hours of the potential exposure.
3	GET TESTED AS SOON AS POSSIBLE PIP does not protect against sexually transmitted infections (STIs) or pregnancy. Make an appointment with your PIP provider within 7-10 days of initiating your medication to complete routine bloodwork including STI screening.
4	GET TESTED AGAIN See your PIP provider again 3-4 months after your exposure to complete routine bloodwork and STI screening.

REMEMBER:

- Take your medication at around the same time each day.
- If you miss a dose, take it as soon as you remember and continue taking your medications as prescribed. Do not take a double dose.
- If you are also taking mineral supplements (such as calcium, iron, or magnesium), antacids (such as Tums or Maalox), or laxatives (such as Dulcolax, Restoralax, Exlax), you should take your PIP medication at least 2 hours before or 6 hours after.
- You should continue to take your medication even if you experience side effects. Mild side effects are normal, especially during the first few days. If you are concerned about any side effects, continue taking your medication and contact your PIP provider as soon as possible.
- Contact your PIP provider if you have any symptoms of a new HIV infection, such as fever, fatigue, rash, headache, swollen lymph nodes, muscle and joint pain.
- You should use condoms and refrain from sharing any injection drug equipment for at least 3 months after your exposure, and until you receive a confirmatory negative HIV test.

Routine Follow Up Assessment

Patients are encouraged to schedule routine follow-up appointments with their PIP provider every 5-6 months, whether they have used their PIP or not. The routine follow up assessment for PIP is consistent with the follow up assessment for PrEP and is described in Table 3, as well as the Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational post-exposure prophylaxis.[1]

Laboratory Investigations

Routine laboratory evaluations and screening for STIs, creatinine, HIV* and HCV testing, syphilis serology, chlamydia and gonorrhea (GC/CT) screening (oropharynx, rectum, urine), and pregnancy testing, if appropriate.

Clinical Evaluation

HIV risk evaluation, including appropriateness of PIP versus PrEP strategies should be performed at every follow up visit. HIV prevention modalities may be changed based on patients' current HIV risk, projected HIV risk, and/or patient preference. Patients should be provided with adherence counselling and HIV education. Providers should inquire about mental health issues, alcohol or drug use and abuse, and provide linkage to appropriate care if needed.

Follow Up After PIP Use

Patients who initiate PIP are advised to schedule a follow-up appointment with their PIP provider within one week of starting medication, and again 12 to 16 weeks after an exposure, as per PEP follow-up guidelines. See Table 3 for suggested evaluations.

Routine follow-up visit schedule can resume following the initiation of a course of PIP.

*We recommend that testing be conducted with a lab-based fourth-generation HIV test.

TABLE 3: SUGGESTED EVALUATIONS FOR PEP-IN-POCKET (PIP)[1]

	ROUTINE VISITS		IF PIP IS INITIATED	
	Baseline Consultation	6-month Follow Up	7-10 days of PIP initiation	12-16 weeks post-exposure
Laboratory Investigations				
HIV testing*	X	X	X	X
Hepatitis A immunity (total antibody)†	X			
Hepatitis B screen (surface antigen, surface antibody, core antibody) †‡	X			
Hepatitis C antibody	X	X	X	X
GC/CT screening§	X	X	X	X
Syphilis serology§	X	X	X	X
Complete blood count	X			
Creatinine	X	X	X	X
Urinalysis	X			
Pregnancy test (as appropriate)	X	X	X	X
Clinical Evaluation				
Symptoms of HIV seroconversion	X	X	X	X
PIP usage and adherence		X	X	X
Confirm indication for PIP initiation			X	
Indications for PIP vs PrEP as HIV prevention strategy	X	X	X	X
Use of other HIV and STI prevention strategies	X	X	X	X
Presence and management of syndemic conditions	X	X	X	X

** Preferred HIV test is a 4th-generation antibody/antigen combo assay. Those with signs or symptoms of acute HIV should also undergo HIV RNA or pooled nucleic acid amplification test.*

† Hepatitis A and/or B vaccine should be initiated in unvaccinated individuals. Those who remain nonimmune to hepatitis B virus should be rescreened annually.

‡ Individuals with chronic active hepatitis B should be managed in consultation with an expert on hepatitis B virus according to Canadian guidelines.

§ Individuals who have STIs should be offered standard therapy and follow-up as per local guidelines.

Transition Between PIP and PrEP

Patients may fluidly transition between PIP and PrEP based on their evolving HIV risk. Any patients discontinuing daily PrEP due to changes in relationship status, lifestyle, etc. and those who are using on-demand PrEP are advised to consider PIP as a safety net.

Additional Exposures While Using PIP

Individuals who have experienced a potential HIV exposure should use condoms during sex and refrain from sharing injection drug equipment for a minimum of 3 months after their initial exposure and they have received a confirmatory negative HIV test. In the event of an additional exposure while taking ARVs, the following recommendations apply:

> **Day 1-25:** no additional doses needed; complete 28 days of medication.
>
> **Day 27-28:** prescribe additional dose(s) to ensure medication coverage extends to 2 days post-exposure.
>
> **Day 29+:** if there has been any discontinuity in medication (i.e., one or more days without medication), begin a new 28-day course of medication.

Special Considerations

Women & Individuals of Child-Bearing Potential

Current clinical guidelines include women and other individuals of child-bearing potential as appropriate candidates for PEP. Special considerations should be made when choosing a PEP regimen for these individuals; see Table 1: Recommended Drug Regimens for PEP-in-Pocket.

Lactation

Expert consultation with an HIV specialist should be sought for patients who are lactating.

Renal Disease

Expert consultation with an HIV specialist should be sought when using TDF and FTC in patients with impaired creatinine clearance.

Suspected Acute HIV Infection

If acute HIV infection of the exposed individual is suspected, then additional laboratory evaluation with HIV RNA nucleic acid amplification test (if available) or repeat fourth-generation assay 7 to 21 days later should be performed. PEP should not be withheld pending the results of these investigations. If the exposed individual is subsequently found to be HIV positive and has started on PEP, the antiretroviral regimen should be continued, and an HIV expert should be consulted as soon as possible.

Daily PrEP Users

Individuals who are taking daily PrEP as prescribed do not require PEP following a potential HIV exposure. If an individual is non-adherent to PrEP, typically missing more than 2 doses per week, PEP may be considered.

On-Demand / 2-1-1 PrEP Users

Individuals who are taking on-demand PrEP as prescribed do not require PEP following a potential HIV exposure. If on-demand PrEP use was suboptimal, PEP may be considered.

Consider providing individuals using on-demand or 2-1-1 PrEP with a prescription PIP and PIP counselling for instances where exposures could not be anticipated, or drug adherence was suboptimal.

Hepatitis B Infection

Patients with chronic hepatitis B virus infection who require PEP may receive a regimen containing tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), but close clinical and laboratory monitoring for hepatitis flares should be considered upon completion of PEP.

Additional PIP Resources

PIP in the Media

2023 - POZ Article: PEP-in-Pocket Is Another Option for HIV Prevention
2023 - TheBodyPro Video: The Case for PEP-in-Pocket (PIP) as an HIV Prevention Tool
2022 - CATIE News: A large study of HIV pre-exposure prophylaxis finds no new cases of HIV with daily dosing
2021 - CATIE Blog: Preventing HIV during the COVID-19 pandemic. PEP and PIP to the rescue
2019 - CATIE News: A novel HIV prevention approach called PIP in cases with infrequent exposure to HIV
2019 - AIDS Map News: Research supports offering PEP in advance in case of risk
2019 - CATIE Blog: Top HIV/Hepatitis C Stories
2018 - HIV and ID Observations Blog: Is self-administered post-exposure prophylaxis another viable option for HIV prevention?
2018 - CATIE News: On-demand PEP to prevent HIV infection

Select Peer-Reviewed Publications

Li J, Liu Y, Nehl E, Tucker JD. A behavioral economics approach to enhancing HIV preexposure and postexposure prophylaxis implementation. Curr Opin HIV AIDS. 2024

Clifford Rashotte M, Yoong D, Naccarato M, Pico Espinosa OJ, Fisher K, Bogoch II, Tan DH. Appropriate usage of post-exposure prophylaxis-in-pocket for HIV prevention by individuals with low-frequency exposures. Int J STD AIDS. 2023 Nov 14:9564624231215151. Online ahead of print.

Billick MJ, Fisher KN, Myers S, Tan DHS, Bogoch II. Brief Report: Outcomes of Individuals Using HIV Postexposure Prophylaxis-In-Pocket ("PIP") for Low-Frequency, High-Risk Exposures in Toronto, Canada. J Acquir Immune Defic Syndr. 2023 Nov 1;94(3):211-213

Billick MJ, Sheps J, Bogoch II. HIV prevention with postexposure prophylaxis-in-pocket (PIP). BMJ. 2023 Aug 2;382:e076016.

Alghamdi A, Hempel A, Heendeniya A, Clifford-Rashotte M, Tan DHS, Bogoch II. HIV postexposure prophylaxis-in-pocket: long-term follow-up of individuals with low-frequency, high-risk HIV exposures. AIDS. 2020 Mar 1;34(3):433-437.

Wood BR. Prevention of HIV for persons with low-frequency, high-risk exposures: PrEP (preexposure prophylaxis), PEP (postexposure prophylaxis), or 'PIP' (postexposure prophylaxis in-pocket). AIDS. 2020 Mar 1;34(3):481-482

Tumarkin E, Heendeniya A, Murphy P, Placido T, Tan DHS, Bogoch II. Brief Report: HIV Postexposure Prophylaxis-in-Pocket ("PIP") for Individuals With Low-Frequency, High-Risk HIV Exposures. J Acquir Immune Defic Syndr. 2018 May 1;78(1):20-22.

References

1. Tan DHS, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, Kille J, Baril J-G, Cox J, Giguere P, Harris M, Hughes C, MacPherson P, O'Donnell S, Reimer J, et al., 2017. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *Can Med Assoc J 189*: E1448–E1458