

2019 August

# Pre-Exposure Prophylaxis Guidelines Review for Primary Care Practitioners in Saskatchewan

Mike Stuber, BSP

Clinical Pharmacist - HIV

[michael.stuber@saskhealthauthority.ca](mailto:michael.stuber@saskhealthauthority.ca) (306)766-0717

---

## Introduction

Saskatchewan continues to have the highest rates of HIV infection in Canada<sup>1</sup> warranting heightened prevention efforts. Pre-exposure prophylaxis (PrEP) is an important prevention strategy that should be offered as an integral part of an overall risk reduction strategy. PrEP involves the use of antiretroviral medications by confirmed HIV-negative individuals at ongoing risk of HIV acquisition. It is initiated before potential or known HIV exposures. It should be used in conjunction with behavioural risk counselling and other harm reduction interventions.

This document aims to provide a practical overview of PrEP for primary caregivers to assist them. It covers the whole process from patient selection, required investigations, prescribing and ongoing monitoring. Recommendations are based on the Canadian Guideline on HIV Pre-exposure Prophylaxis and Nonoccupational PostExposure Prophylaxis<sup>2</sup>, Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2014<sup>3</sup> and 2018 Alberta HIV Pre-Exposure Prophylaxis (PrEP) Guidelines<sup>4</sup>

---

<sup>1</sup> Population Health Branch, Government of Saskatchewan (2017). *HIV Prevention and Control Program Report for 2017*. Retrieved from <http://www.saskatchewan.ca/government/government-structure/ministries/health/other-reports/annual-report-archive#step-4>

<sup>2</sup> CMAJ 2017 November 27;189:E1448-58. doi: 10.1503/cmaj.170494

<sup>3</sup> Centres for Disease Control (2014). Retrieved from <https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf>

<sup>4</sup> Alberta Health Services (citation)

---

---

## Note:

- Pre-Exposure Prophylaxis in this document refers to the use of fixed-dose combination tablet of ***tenofovir disoproxil fumarate/emtricitabine (300mg/200mg)*** [Truvada<sup>®</sup>, generics].
  - Generic products are available at *no cost* (including dispensing or professional fees) to residents with an active Saskatchewan Health Card or who are covered under Non-Insured Health Benefits (NIHB).
  - Tenofovir DF/emtricitabine is an open benefit on the Saskatchewan Drug Plan Formulary and requires no Exception Drug Status application.
  - Tenofovir alafenamide/emtricitabine (Descovy<sup>®</sup>) is not currently approved for use as PrEP.

## Recommendations

### I General:

PrEP is part of a comprehensive approach to HIV prevention that includes behavioural interventions such as proper condom usage and risk reduction counselling and providing therapies, services and supplies that aim to reduce the risk of acquiring an infection that is both sexually transmitted and bloodborne. Harm reduction should be offered in addition to PrEP when possible and includes, but is not limited to, sterile drug use equipment distribution, addictions counselling and opioid substitution therapy.

As a preventive intervention PrEP can be offered in a variety of health care settings in order to increase access. Physicians, nurses/nurse practitioners and pharmacists, where scope of practice allows or collaborative prescribing agreements in place, can initiate and provide follow-up for PrEP. Non-prescribing health care providers should be encouraged to educate themselves on PrEP in order to help identify candidate patients as well as assist in monitoring and adherence support.

PrEP providers must be familiar with local HIV care providers in order to provide rapid linkage to care for those who test HIV positive during initial assessment or follow-up. A map of services can be found at the Saskatchewan HIV Collaborative website (<https://www.skshiv.ca/map-of-services>).

---

## II Patient Identification:

PrEP patients fall into three categories: 1) men who have sex with men (MSM) and transgender women (TGW); 2) heterosexuals; and persons who inject drugs (PWID) (See **Appendix A**).

### MSM and TGW

**HIV negative MSM and TGW who report condomless anal sex within the last 6 months should be considered for PrEP and counselled on risk reduction**

- PrEP is recommended for the above if:
  - Infectious syphilis or rectal bacterial STI (gonorrhea or chlamydia) especially if in last 12 months
  - Use of non-occupational Post Exposure Prophylaxis (nPEP) more than once
  - Ongoing sexual relationship with HIV positive partner(s) with significant risk of transmissible HIV. (See **Appendix B**).
- The HIV Incidence Risk Index for MSM (HIRI-MSM) is a tool to assess risk of HIV acquisition (see **Appendix B**) A score greater than 11 is a compelling indication for PrEP. However, a score less than 11 does not preclude the use of PrEP in Saskatchewan.
  - Higher scores are associated with:
    - **Receptive anal sex without a condom**
    - Any HIV+ partners
    - Ages 18-40
    - 6 or more partners in the last 6 months
    - Use of methamphetamines
- **PrEP is not indicated in the context of a stable closed/monogamous relationship with a single partner with no/negligible risk of having transmissible HIV (i.e. HIV negative, HIV positive with viral load <40 copies/mL).**<sup>5</sup>

---

<sup>5</sup> Centers for Disease Control and Prevention (Sept 27, 2017). Dear Colleague [Letters]. Retrieved from <https://www.cdc.gov/hiv/library/dcl/dcl/092717.html>

---

Many MSM and TGW are aware of PrEP but may not discuss this with their healthcare providers due to stigma. Due to access concerns many may seek out PrEP via informal methods (mail/internet order, inappropriate use of post-exposure prophylaxis or buying/borrowing from HIV positive contacts). These informal methods carry inherent risks including questionable quality of drugs, inconsistent supply leading to poor adherence, lack of counselling, monitoring and potential for seroconversion with development of drug resistant virus.<sup>6</sup>

### Heterosexuals

- PrEP is indicated for the HIV negative partner in a heterosexual relationship with an HIV+ person if the HIV+ **has a significant risk of having transmissible HIV** and where condoms are not used consistently. See **Appendix B** for risk assessment.
- PrEP may be considered for the HIV negative partner of an HIV+ person where the HIV+ has a **non-negligible risk of having transmissible HIV**. This includes HIV negative individuals attempting to conceive with an HIV+ partner.
- PrEP should be considered in pregnant women who are at risk of HIV acquisition in order to reduce the risk of seroconversion and subsequent vertical transmission of HIV.

### Persons Who Inject Drugs (PWID)

- PrEP should be considered for persons who inject drugs if they are at risk of HIV infection.
  - In Saskatchewan, IDU is the most common HIV transmission route.<sup>7</sup> People who inject drugs should be considered for PrEP in most areas of the province.
- Although not validated for use in Saskatchewan, the ARCH-IDU Risk Score (see **Appendix C**) may be useful for screening PWID for PrEP.
- Sterile drug use equipment distribution programs, medication assisted treatments for substance use disorders (methadone, suboxone, etc) and other harm reduction techniques should be used in conjunction with PrEP if available.

---

<sup>6</sup> Brisson, J (2017). *Ethical public health issues for the use of informal PrEP*. *Global Public Health*, 03 Sept 2017, pp 1-6

<sup>7</sup> Population Health Branch, Government of Saskatchewan (2015). HIV Prevention and Control Program Report for 2015. Retrieved from <http://www.saskatchewan.ca/government/government-structure/ministries/health/other-reports/annual-report-archive#step-4>

- 
- PrEP can be dispensed along with opioid substitution therapy in patients who continue to inject.
  - Pregnant women who inject drugs should be considered for PrEP in order to reduce the risk of HIV infection and subsequent vertical transmission to infant.

### III Initial Evaluation:

Requirements for PrEP:

- **HIV negative** within last 5 to 14 days
- **eGFR >60mL/min** and no underlying renal dysfunction
  - PrEP is contraindicated in people with renal dysfunction (eGFR less than 60 mL/min). Refer to Infectious Diseases specialist.

PrEP is only indicated for people with **confirmed HIV negative status**.

- Confirm HIV status with standard laboratory testing (4th generation assay)
- Evaluate for signs and symptoms suggestive of acute HIV infection in the last 12 weeks. See **Appendix B**.
  - If acute HIV suspected defer PrEP and repeat 4th generation assay one to three weeks later. Use clinical judgement if patient is at high, ongoing risk of HIV infection.
- Consider Post Exposure Prophylaxis (PEP) for patients presenting with high risk exposure within the last 72 hours.

Other tests:

- Pregnancy test should be done at baseline in individuals of childbearing potential.
- Laboratory screening for STIs (gonorrhoea, chlamydia and syphilis) including extra-genital sites (throat, rectum) as indicated by sexual activity.
- Viral hepatitis investigations should be done at baseline:
  - **Hepatitis A:** Immunize if non-immune

- 
- **Hepatitis B:** TDF/FTC is active against HBV. Treatment interruptions or discontinuation may result in rebound viremia and worsening of symptoms. Patients with HBV infection should be made aware. Patients negative for HBV should be immunized.
    - Consult Canadian Hepatitis B treatment guidelines or Infectious Diseases specialist for patients with chronic HBV infection
  - Hepatitis C: refer to HCV treatment guidelines or Infectious Diseases specialist for follow-up.

**Discussion:**

- Review patient's sexual and substance use history
- Review the patient's current HIV risk reduction strategies. Provide education on proper condom use, safer injection techniques and refer for substance use disorder treatment if needed. See **Appendix B.**
- Counsel on PrEP dosing, importance of adherence and how to manage adverse effects. (See **Appendix D)**
- Most common adverse effects when initiating PrEP include:
  - Nausea, stomach upset
  - Headache
  - Weight loss
- Longer term or serious adverse effects include:
  - Decrease in bone mineral density that appears reversible on discontinuation<sup>8</sup>
  - Decrease in kidney function that generally resolves on discontinuation
  - Lactic acidosis
- While PrEP resistance remains rare, there have been a very small number of cases reported in the literature. Due to the antiretroviral activity of PrEP agents, HIV infection while on PrEP may present atypically.

---

<sup>8</sup> Glidden, DV et al (2017). Brief Report: Recovery of Bone Mineral Density After Discontinuation of Tenofovir-Based HIV Pre-Exposure Prophylaxis. *J Acquir Immune Defic Syndr.* 2017 Oct 1;76(2):177-182. doi: 10.1097/QAI.0000000000001475

- 
- Drug coverage
    - PrEP is covered 100% for all Saskatchewan residents with active health cards or coverage under NIHB.
      - Patients should receive **generic** tenofovir/emtricitabine **at no cost**, including markup, dispensing fee or private insurance coverage.
      - Patients without active Saskatchewan Health coverage must apply for a card:  
<https://www.ehealthsask.ca/residents/health-cards/Pages/Apply-for-a-Health-Card.aspx>
  - Ensure patient is aware of monitoring and follow up protocol in order to continue PrEP.
    - Patient must be able to commit to regular laboratory investigations (HIV, STI and serum creatinine) every 3 months.
    - Provide patient with follow up appointment, or
    - Provide patient with laboratory requisitions ‘standing orders’ and instructions when to complete required investigations

#### IV PrEP Prescription

- **“Generic Truvada<sup>®</sup> one tablet once daily for HIV prophylaxis”**
  - **30 day supply and two refills**
  - **Prescription expires 3 months from the date written**
    - This limits potential for patients to resume PrEP intermittently without necessary monitoring and follow up. See sample prescription (**Appendix E**) and information for pharmacy (**Appendix F**).
- Alternative “on demand” dosing indicated **only for Men who have sex with Men** who engage in sporadic or intermittent high risk behaviours and who demonstrate a thorough understanding of an on demand regimen. **This regimen is very rarely indicated and thorough patient education and counselling must be undertaken before pursuing this option.**
  - “Truvada<sup>®</sup> two tablets 2-24 hours prior to HIV exposure followed by one tablet daily until 48 hours after last sexual exposure”

- 
- Risk of seroconversion if PrEP not taken before each sexual encounter and subsequent potential for the development of drug resistant HIV.
  - Linking PrEP to opioid substitution therapy may be a useful strategy to promote adherence.

## V PrEP Follow Up

Ongoing provision of PrEP is dependant on regular laboratory evaluations.

Day 30:

- HIV test to rule out infection in 'window period' at baseline evaluation
- Serum creatinine to assess renal response to medication

Every 90 days thereafter:

- HIV test
- Serum creatinine to assess renal response
- STI screening (include urethral, rectal and throat swabs as needed based on patient sexual history)
- Pregnancy test in women of childbearing age

Patients should establish schedule for regular laboratory evaluation before they run out of supply of medication in order for results to be available to prescriber in a timely fashion. Laboratory requisitions should be pre-drawn up and given to patient to facilitate follow up. **Prescriptions should not be renewed until prescriber has reviewed results and determined that patient remains HIV negative and renal function remains greater than 60 mL/min.**

Opioid substitution therapy patients can have HIV and serum creatinine screens coordinated with other regular lab work when possible.

Chaotic lifestyles may add complexity to PrEP follow up. Arranging dates and locations to draw lab work and flexibility on the part of the prescriber may facilitate continuation of PrEP. Prescribers must weigh risks and benefits of continuing PrEP in patients who may be at risk of HIV infection but does not complete required lab work on a routine basis.



---

Guidelines suggest seeing patients every 3 to 6 months for follow up. Prescribers should assess changes in risk behaviours to determine if PrEP is still indicated, assess adherence and determine tolerability and affordability. Stable patients with good adherence to medication and laboratory follow up this may be reduced to every 6-12 months after initial 90 day visit at prescriber discretion. Telephone follow up may be a useful option.

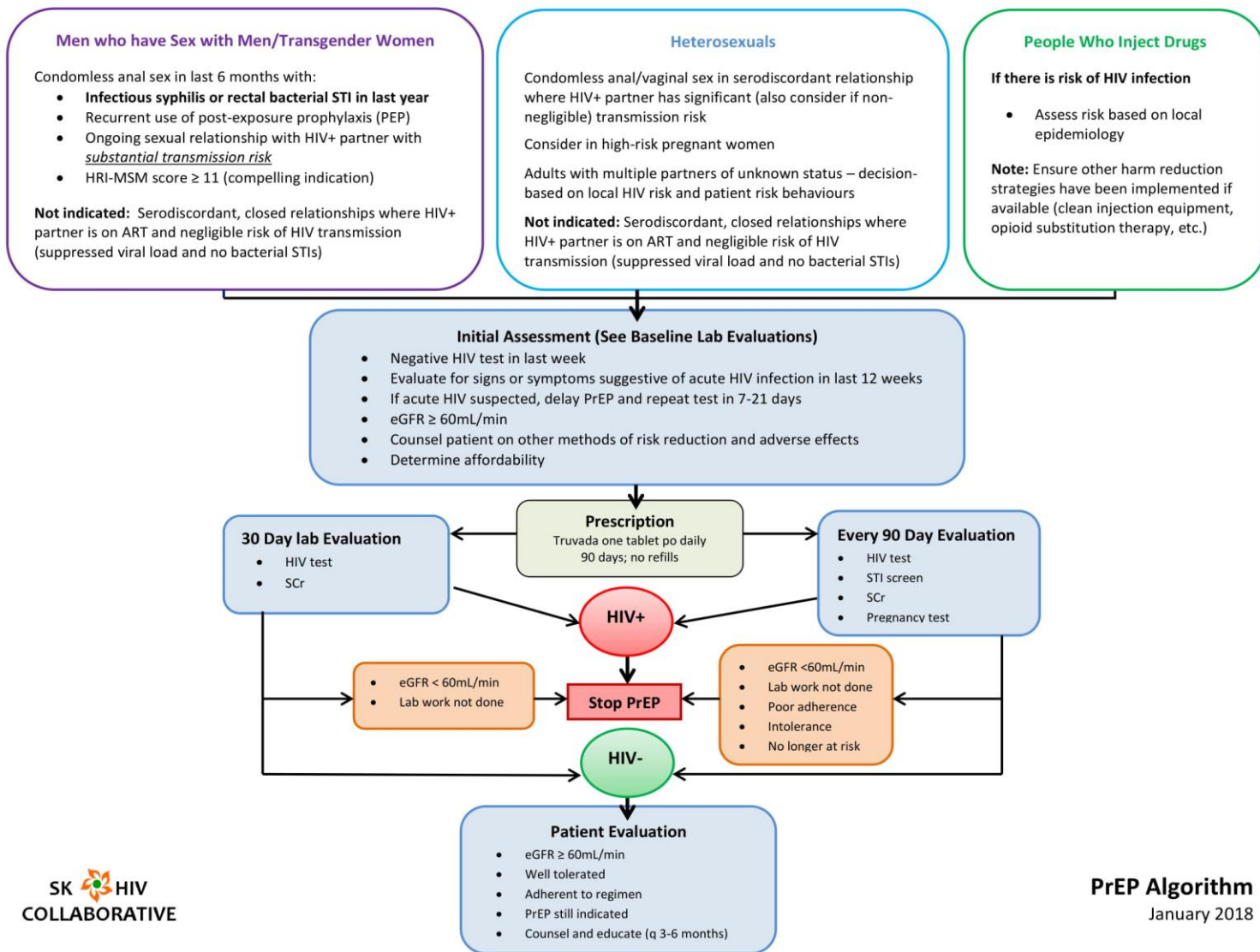
## VI PrEP Discontinuation

- To discontinue PrEP when no longer indicated, guidelines suggest stopping 2-28 days after last high risk sexual exposure. Prescribers should use clinical judgement and patient interview to determine appropriate time frame.
- Follow up HIV testing should be performed at up to 8 weeks post discontinuation.
- Patients with chronic HBV infection should be monitored in accordance with HBV treatment guidelines as discontinuation of PrEP may result in reactivation of chronic HBV infection.


## VII Summary

- Ensure HIV negative status prior to PrEP start and repeat HIV testing every 90 days
- Contraindications include positive HIV test and serum creatinine less than 60mL/min
- Prescribe PrEP for up to 90 days and *indicate prescription expires 90 days from day written*
- Routine laboratory evaluations required to be completed and reviewed prior to prescription renewal. Clinical judgement and weighing risks and benefits must be made prior to discontinuing PrEP in patients who don't complete routine lab work on time
- Detailed information regarding PrEP can be found on the SK HIV Collaborative website at [www.skshiv.ca](http://www.skshiv.ca)
- Leveraging Immediate Non-urgent Knowledge (LINK) is a telephone consultation service to give primary care providers rapid access to specialists to discuss less serious patient conditions. Call: 1-844-855-LINK (5465) to access an infectious disease specialist if you have any questions about PrEP.

## Appendix A: PrEP Algorithm (Front of Card)



## Appendix B: PrEP Algorithm (back of card)

 <b>PrEP: Quick Reference</b>					For More: SKHIV.ca			
Baseline and Follow Up Evaluations					<b>HIV Incidence Risk Index for MSM (HIRI-MSM) Score ≥ 11 = Compelling</b>			
Assay Type	Baseline (Day 0)	Day 30	Every 3 months	Annual	Question	Response	Score	
HIV testing	✓	✓	✓		How old are you today (years)?	<18 <b>18-28</b> <b>29-40</b> 41-48 >48	0 <b>8</b> <b>5</b> 2 0	
Hepatitis A immunity (hepatitis A IgG) <ul style="list-style-type: none"> <li><b>Vaccine should be initiated in unvaccinated individuals</b></li> </ul>	✓				How many men have you had sex with in the <b>last 6 months?</b>	≥10 <u>male partners</u> 6-10 male partners 0-5 male partners	<b>7</b> 4 0	
Hepatitis B screen (surface antigen, surface antibody, core antibody) <ul style="list-style-type: none"> <li><b>Vaccine should be initiated in unvaccinated individuals</b></li> <li>Chronic active HBV should be managed appropriately</li> </ul>	✓				How many of your male sex partners <b>were HIV positive?</b>	≥1 <u>positive partner</u> 1 positive partner <1 positive partner	<b>8</b> 4 0	
Hepatitis C antibody <ul style="list-style-type: none"> <li>Refer or treat if needed</li> </ul>	✓			✓	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man without a condom?	<b>1 or more times</b> 0 times	<b>10</b> 0	
Gonorrhea & chlamydia screen <ul style="list-style-type: none"> <li>Urine NAAT, throat and rectal swabs for culture/NAAT according to sexual activity</li> </ul>	✓		✓		In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	<b>5 or more times</b> 0 times	<b>6</b> 0	
Syphilis serology	✓		✓		In the last six months, have you used <u>methamphetamines</u> such as crystal or speed	<b>Yes</b> No	<b>5</b> 0	
Complete blood count	✓				In the last 6 months have you used <u>poppers</u> (amyl nitrate)?	<b>Yes</b> No	<b>3</b> 0	
Creatinine	✓	✓	✓		Signs and Symptoms of Acute HIV Infection			
Urinalysis	✓				Sign/Symptom	%	Sign/Symptom	%
Pregnancy test as appropriate	✓		✓		Fever	<b>53-90</b>	Lymphadenopathy	<b>7-75</b>
					Weight loss/anorexia	<b>46-76</b>	Pharyngitis	<b>15-70</b>
					Fatigue	26-90	Myalgia or arthralgia	<b>18-70</b>
					Gastrointestinal upset	<b>31-68</b>	Aseptic meningitis	24
					Rash	9-80	Oral ulcers	10-20
					Headache	32-70	Leukopenia	40

## Appendix C: ARCH-IDU Risk Score

### ARCH-IDU Scoring Sheet

How old are you today (years)?	If <30 years If 30-39 years If 40-49 years If ≥50 years	Score 38 Score 24 Score 7 Score 0			_____
In the last 6 months, were you in a methadone maintenance program?	If yes, If no,	Score 0 Score 31			_____
In the last 6 months, how often did you inject heroin?	If 1 or more times If 0 times	Injection sub-score 1 Injection sub-score 0		_____	
In the last 5 months, how often did you inject cocaine?	If 1 or more times If 0 times	Injection sub-score 1 Injection sub-score 0		_____	
In the last 6 months, how often did you share a cooker?	If 1 or more times If 0 times	Injection sub-score 1 Injection sub-score 0		_____	
In the last 6 months, how often did you share needles?	If 1 or more times If 0 times	Injection sub-score 1 Injection sub-score 0		_____	
In the last 6 months, how often did you visit a shooting gallery?	If 1 or more times If 0 times	Injection sub-score 1 Injection sub-score 0		_____	
Composite Injection Score			Add down the injection sub-scores above		
			If 0 If 1 If 2 If 3 If 4 If 5	Score 0 Score 7 Score 21 Score 24 Score 24 Score 31	_____
	Add down the three entries in the right column to calculate total score				<b>Total Score:</b>

To identify active IDU in their practice, we recommend clinicians ask all patients a routine question: “Have you ever injected drugs that were not provided by a physician”. If yes, “When was the last time you injected any drugs?” Only complete the risk index if they have injected any nonprescription drug in the last 6 months.

If score is 46 or greater, evaluate for PrEP or other intensive HIV prevention services for IDU.

If score is 45 or less, provide standard HIV prevention services for IDU.

<sup>1</sup> Smith, D., Pan, Y. et al. (2015). A briefing tool to assess the risk of contracting HIV infection among active injection drug users. *Journal of Addiction Medicine*, 9(3), pp. 226-232.



---

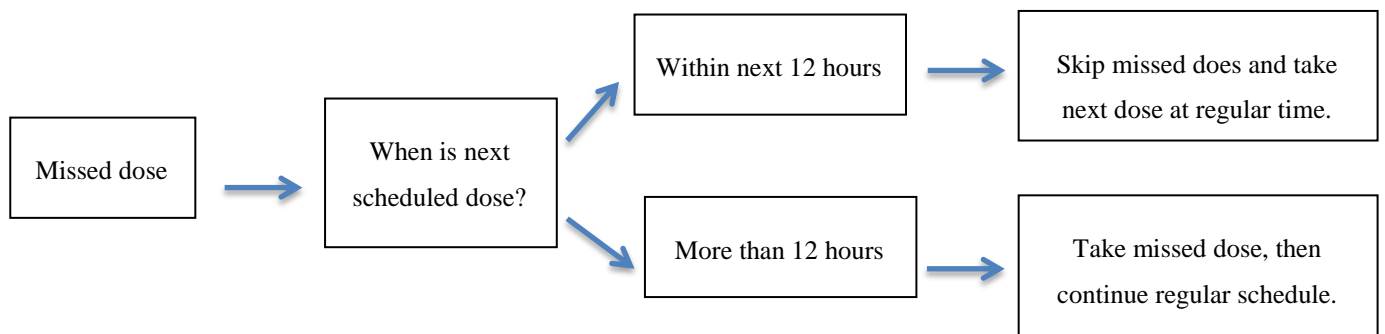
## Appendix D: PrEP FAQs

### How effective is PrEP?

Using PrEP can lower your risk of getting HIV by 92-99% (compared to not taking PrEP). PrEP is most effective when taken every day.

*[92% comes from a secondary analysis in the iPrEx study that compared people who had detectable drug levels in their body versus those who did not, all within the group assigned to take PrEP. 99% comes from the iPrEx Open-Label Extension that used tenofovir concentrations in dried blood samples to correlate with adherence (# of tablets per week)—no HIV infections were detected in those who took at least 4 tablets per week.]*

### What to do if patient misses doses?

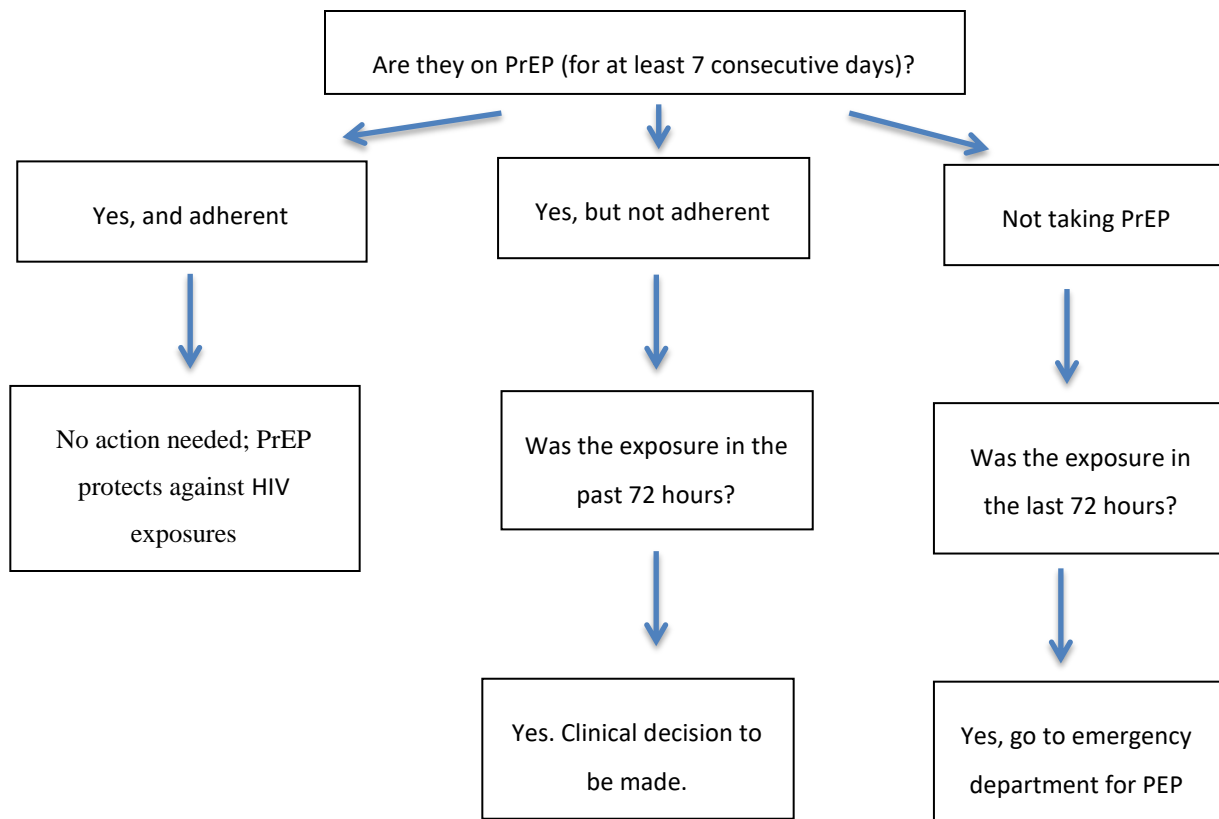


If patient missed 3 or more doses:

- It will take 7 consecutive days of PrEP to build up to protective drug levels again → encourage condom use or safer sex techniques

---

### What to do if the patient had an HIV exposure



### What is on-demand dosing of PrEP?

On Demand dosing may be appropriate for select patients. Based on available evidence, on-demand dosing can only be considered in men who have sex with men.

**On-demand dosing, take two pills together 2-24 hours before the first sexual exposure to HIV, followed by one pill once daily until 48 hours after the last sexual activity. On-demand dosing of PrEP should not be initiated without prior consultation with a health care provider.**

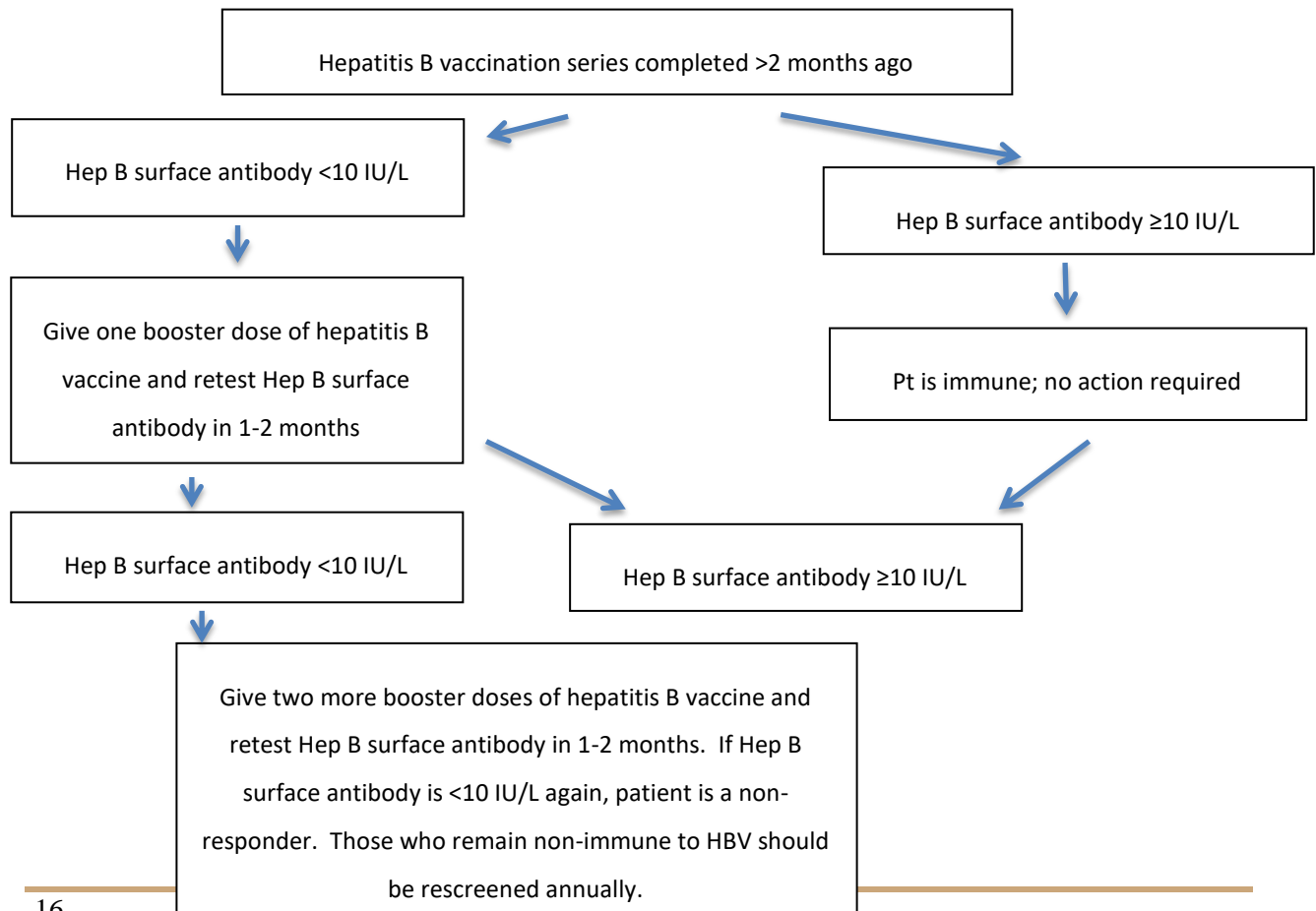
---

### When can on-demand dosing of PrEP be used?

On-demand may be considered to decrease pill burden in those who have infrequent sexual exposures. Patients being considered for On-Demand dosing must be aware of the need to take the regimen as prescribed and how to manage exposures when PrEP has not been taken. Patients will still need to be tested as per guidelines for daily dosing. Counselling patients on On-Demand dosing should include risks of HIV infection and reduced efficacy compared to daily dosing.

### What to do if patient had completed the hepatitis B vaccination series, but surface antibody screening result is “non-immune”, i.e. <10 IU/L?

“Non-immune” results of hepatitis B surface antibody screening only confirm no immune response if done 1-2 months after the last vaccination. See flowchart below for testing hepatitis B surface antibody >2 months after the last vaccination:





---

## Appendix E: Sample Prescription

Rx - **TRUVADA TABLET (200-300 MG)** (*emtricitabine/tenofovir disoproxil fumarate*)

1 (One) Tablet(s), Once daily X 30 Day(s)

*Pharmacist Instructions:*

For HIV Pre-Exposure Prophylaxis

Note: Prescription EXPIRES 3 months from the day written and patient must repeat lab work before refill allowed.

Qty: 30 (Thirty) Tablet(s)

Refills: 2

Start Date: 01-Jan-2019

Compliance Pkg Req: No

Effective Date: 01-Jan-2019

Drug Use: Continuous

Route: Oral

End Date: 01-Apr-2019

Substitutions: Allowed

Expiry Date: 01-Apr-2019

Trial Dispenses: Not Authorized

---

## Appendix F: Sample Fax to Pharmacy

### A patient of your pharmacy is initiating HIV pre-exposure prophylaxis (PrEP)

#### What is PrEP?

Tenofovir disoproxil fumarate 300 mg/Emtricitabine 200 mg (Truvada<sup>®</sup>) is indicated as a once-daily regimen for prevention of HIV in confirmed HIV-negative individuals. Patients taking PrEP should have lab tests completed before starting PrEP, 30 days after starting PrEP, as well as every 3 months as part of follow-up. Prescription renewals are provided upon reviewing results of each 3-month follow-up of lab tests. Please review lab results on eHealth viewer to confirm this medication is being used in accordance with guidelines: [www.skhiv.ca/pre-exposure-prophylaxis-prep/](http://www.skhiv.ca/pre-exposure-prophylaxis-prep/)

#### Issuing pharmacist-prescribed interim supplies:

PrEP is prescribed for a maximum of 90 days and patients are reminded to complete follow-up lab tests 7-10 days before they are out of medications. If a patient has run out of medications, they are advised to complete their lab tests and contact their health care provider. If an interim supply is provided, please notify the prescriber by faxing a refill authorization request to (306) XXX-XXXX. Encourage the patient to have their testing done and review lab results prior to dispensing.

#### For more information:

- [www.skhiv.ca](http://www.skhiv.ca)
- <https://www.catie.ca/en/fact-sheets/prevention/pre-exposure-prophylaxis-prep>
- Canadian HIV prophylaxis guidelines: <http://www.cmaj.ca/content/cmaj/189/47/E1448.full.pdf>

*Insert Health care provider information here:*

*Name*

*Address*

*Phone/Fax number*