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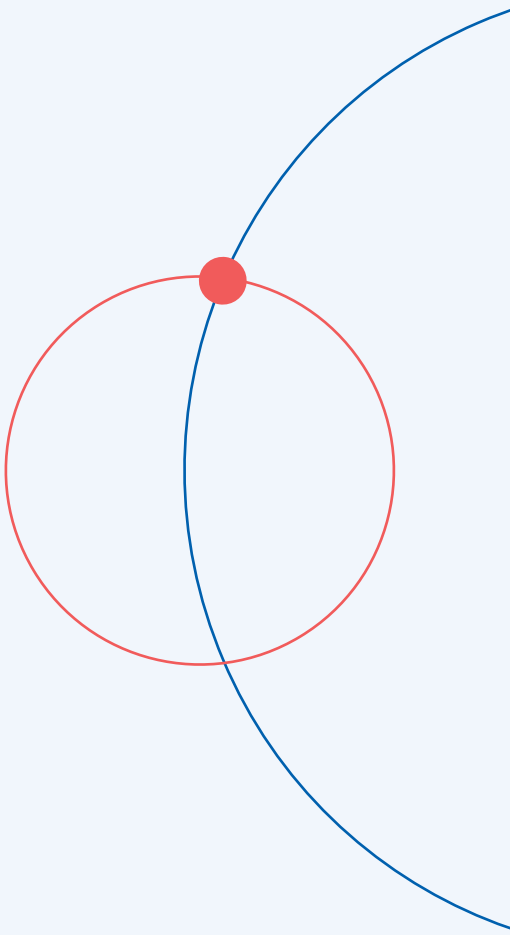

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Acknowledgements

PrEP GUIDELINES PANEL

Chair Guidelines Panel: Prof Edwina Wright

Infectious Diseases Specialist, Department of Infectious Diseases, Monash University Central Clinical School, Honorary Principal Fellow, Burnet Institute, Honorary Associate Professor, Peter Doherty Institute for Infection and Immunity, Melbourne, VIC

Dr Ian Anderson

Sexual Health Advanced Trainee, Associate Lecturer at University of Queensland and

University of New South Wales

Dr Benjamin Bavinton

Senior Research Fellow and Group Leader, Biobehavioural Prevention Group, The Kirby Institute, UNSW Sydney, NSW

Dr Charlotte Bell

Consultant Sexual Health Physician, Adelaide Sexual Health Clinic, SA

Dr Doris Chibo

Senior Scientist, Victorian Infectious Diseases Reference Laboratory

Dr Vincent Cornelisse

Staff specialist in sexual health medicine, RPA Sexual Health and Clinic 16, NSW Health.

Conjoint senior lecturer, The Kirby Institute for Infection and Immunity in Society, UNSW

Prof Andrew Grulich

Head, HIV Epidemiology and Prevention Program, The Kirby Institute, UNSW Sydney, NSW

Dr Nicholas Medland

The Kirby Institute, UNSW Sydney, NSW

Dash Heath-Paynter

Deputy CEO, Health Equity Matters, Sydney, NSW

A/Prof Darren Russell

Director of Sexual Health, Cairns Sexual Health Service, and James Cook University, QLD

Dr Eloise Williams

Clinical Microbiologist and Infectious Diseases Specialist, Victorian Infectious Diseases Reference Laboratory

A/Prof Iryna Zablotska-Manos

HIV epidemiologist, the Sydney Medical School – Westmead, Faculty of Medicine and Health, The University of Sydney, NSW

ASHM PrEP GUIDELINES SECRETARIAT

Neal Steetsel

Project Officer, ASHM, NSW

REVIEWING COMMITTEE

HIV National Advisory Group

ASHM

HIV Sexual Health Advisory Group

ASHM

Dr Mark Bloch

Director Holdsworth House Medical Practice, Conjoint A/Prof UNSW, Sydney, NSW

Phinn Borg

Executive Director of The Gender Centre, Sydney, NSW

Dr Adam Bourne

Associate Professor, Australian Research Centre in Sex, Health & Society,

La Trobe University, Melbourne, VIC

Prof Mark Boyd

MD, FRACP, Chair of Medicine, Lyell McEwin Hospital, University of Adelaide. Research Director, Northern Adelaide Local Health Network (NALHN), SA Health. Principal Research Fellow, SAHMRI. Visiting Professorial Fellow, Kirby Institute UNSW Australia. Co-Editor-in-Chief, AIDS Research and Therapy, SA

Jude Byrne

National Coordinator of Peer Programs, AIVL, Canberra, ACT

Teddy Cook

Director, Community Health, ACON, Sydney, NSW

Prof. Benjamin Cowie

Director, WHO Collaborating Centre for Viral Hepatitis, Doherty Institute, Royal Melbourne

Hospital, and Department of Medicine, University of Melbourne, Melbourne, VIC

Dr Pauline Cundill

General Practitioner and Medical Educator, Pandanus Medical NT and Northern Territory

General Practice Education, Darwin, NT

A/Prof Philip Cunningham

Chief Operating Officer, NSW State Reference Laboratory for HIV, Centre for Applied Medical Research, St Vincent's Hospital, Sydney, NSW

Dr Robert Finlayson

Director, Sexual Health Medicine, Taylor Square Private Clinic, Sydney, NSW

Sally Goldner

AM, Educator and Treasurer, Transgender Victoria Inc, Melbourne, VIC

A/Prof Michelle Giles

MBBS FRACP PhD, The Alfred Hospital, Royal Women's Hospital, Monash Health and Sunshine Hospital, VIC

A/Prof David Gracey

Renal Unit, Royal Prince Alfred Hospital, Central Clinical School, Faculty of Medicine, University of Sydney, NSW

Dr Manoji Gunathilake

Sexual Health Physician, Sexual Health & Blood Borne Virus Unit, Northern Territory Department of Health, Darwin, NT. Sexual Health Programme, Kirby Institute, UNSW, Sydney, NSW

Jo Holden

Director, Population Health Strategy & Performance, Centre for Population Health, NSW Ministry of Health, NSW

Hollie Johnson

Clinical Nurse Consultant, Keeping the Body in Mind Program, Eastern Suburbs Mental Health Service-SESLHD, NSW

Kirsty Machon

Executive Officer, Positive Women Victoria, Melbourne, VIC

Prof Lisa Maher

Program Head, Kirby Institute for Infection and Immunity, UNSW Sydney, NSW

A/Prof Lewis Marshall

South terrace Clinic Infectious Diseases Dept Fremantle Hospital, WA

Dr Anna McNulty

Director, Sydney Sexual Health Centre, South Eastern Sydney Local Health District, NSW

Dr Dean Murphy

Senior Research Fellow Australian Research Centre in Sex, Health and Society, La Trobe University, Melbourne

Dr Catriona Ooi

Clinical Director Sexual Health, Northern Sydney Sexual Health Service: Clinic 16,

Royal North Shore Hospital, St Leonards, NSW

Dr Mark O'Reilly

Director Prahran market clinic, Melbourne, VIC

Clinical A/Prof Louise Owen

MBBS (Hons) FRACGP FAChSHM Sexual Health Physician, Director, State-wide Sexual Health Service, Hobart, TAS

Mish Pony

CEO, Scarlet Alliance, Australian Sex Workers Association

Dr Clara Tuck Meng Soo

Practice Principal, East Canberra General Practice

Shannon Woodward

Nurse Practitioner, Canberra Sexual Health Centre, Canberra Health Services ACT

COPY EDITOR

Mary Sinclair

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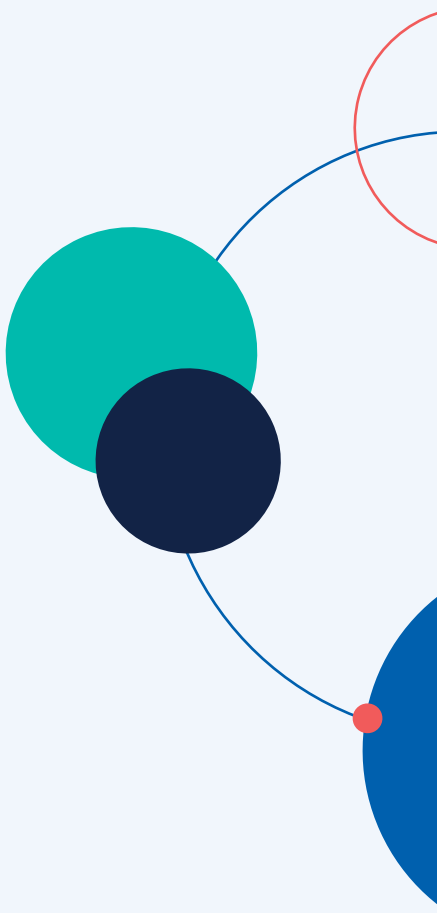

Glossary

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARTG	Australian Register of Therapeutic Drugs
BMD	bone mineral density
eCrCl	estimated creatinine clearance rate
eGFR	estimated glomerular filtration rate
GAHT	gender-affirming hormone therapy
FTC	emtricitabine (trade name Emtriva)
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
iPrEx	Pre-exposure Prophylaxis Initiative
MSM	men who have sex with men
nPEP	non-occupational post-exposure prophylaxis
NSP	needle and syringe program
OST	Opioid Substitution Therapy
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PCR	urine protein: creatinine clearance
PEP	post-exposure prophylaxis
PrEP	pre-exposure prophylaxis
PIS	Personal Importation Scheme
PoCT	point-of-care test
PWID	people who inject drugs
s100	a section of the Pharmaceutical benefits Scheme which provides access to highly specialised drugs
STI	sexually transmissible infection
TD*	tenofovir disoproxil maleate or fumarate or phosphate
TDF	tenofovir disoproxil fumarate (trade name Viread)
TDM	tenofovir disoproxil maleate (trade name Trucitavir)
TDP	tenofovir disoproxil phosphate (trade name Tenofovir EMT Lupin
TDF/ FTC	tenofovir disoproxil fumarate coformulated with emtricitabine (trade name Truvada, or in generic form Tenvir). In Australia, the TGA has also approved the generic Trucitavir, which is coformulated tenofovir disoproxil maleate and emtricitabine and Tenofovir EMT Lupin which is co-formulated tenofovir disoproxil phosphate and emtricitabine
TFV-DP	tenofovir diphosphate
TGA	Therapeutic Goods Administration
TGM	Transgender Men
TGW	Transgender Women
WHO	World Health Organization

1. Introduction

Widespread availability and uptake of human immunodeficiency virus (HIV) preexposure prophylaxis (PrEP) has the potential to significantly reduce HIV transmission in Australia and globally.

Co-formulated tenofovir and emtricitabine for use as HIV pre-exposure prophylaxis (PrEP) by people at risk of HIV infection is recommended as standard care in clinical guidelines in the United States of America, Europe and Australia **(1, 2, 3)**, as well as globally through World Health Organization (WHO) guidelines **(4)**. When used with optimal medication adherence, daily PrEP is a highly effective HIV prevention strategy for men who have sex with men (MSM), heterosexual men and women, transgender people, and people who inject drugs who are at-risk of HIV acquisition **(5-11)**. In addition, on-demand† PrEP has been demonstrated to be highly effective in MSM and has also been recommended by the World Health Organisation as a dosing option for other populations (see suitability criteria).

These clinical PrEP guidelines update the 2023 ASHM PrEP guidelines **(3)** which were initially an adaptation and update of the 2014 United States Centers for Disease Control's PrEP guidelines **(16)**.

On May 2016, the Australian Therapeutic Goods Administration (TGA) approved the entry of Truvada (coformulated tenofovir disoproxil fumarate and emtricitabine TDF/FTC; Gilead Sciences) onto the Australian Register of Therapeutic Goods (ARTG) for HIV PrEP for people at risk of HIV infection. Since then, a number of generic co-formulations of tenofovir disoproxil* and FTC have been registered by the TGA for HIV PrEP (for simplicity, TD* is used in these guidelines to denote the tenofovir disoproxil component present in the medicines registered for PrEP use in Australia).

From 1 April 2018, the brand and generic versions of TD*/FTC became available through the Australian Pharmaceutical Benefits Scheme (PBS) at subsidised cost for HIV PrEP **(17)**. Whereas previously PrEP was available only through clinical trials, private scripts or through personal importation, it can now be prescribed by all general practitioners (GP) and authorised nurse practitioners using PBS scripts. People with Medicare numbers can fill their scripts through the PBS, however people who are Medicare ineligible can either legally import generic PrEP using the TGA Personal Importation Scheme (PIS) **(18)** or pay the full price with a private script.

The recommendations in these guidelines are designed to:

- support the prescribing of PrEP using either ARTG-listed and PBS subsidised drugs, or the same or other generic drugs that are available through personal importation, or by paying the full price with a private script
- assist clinicians in their evaluation and HIV risk assessment of patients who are seeking PrEP
- assist clinicians in initiating their patients on PrEP by providing information on PrEP dosing schedules
- assist clinicians in the monitoring of patients on PrEP, including testing requirements and management of side-effects and toxicity
- assist clinicians to be aware of more complex situations such as the use of PrEP in pregnancy and in chronic hepatitis B infection
- assist clinicians in understanding how to safely cease PrEP.

These guidelines are intended for use by:

- general practitioners who provide care to people at risk of acquiring HIV infection
- sexual health physicians and ID physicians who provide care to people at risk of acquiring HIV infection and/or who serve as consultants to primary-care physicians about the use of ARV antiretroviral treatment
- infectious disease and HIV treatment specialists who may provide PrEP for, or serve as consultants to primary-care physicians about the use of antiretroviral medications
- trainees and registrars in each of the above categories
- authorised nurse practitioners who provide care to people at risk of acquiring HIV infection
- nurses working in nurse-led clinics in consultation with doctors
- peer workers
- counsellors and people performing HIV testing, including point-of-care testing
- health program policymakers
- health consumers and others with an interest in HIV PrEP.

Key recommendations of the ASHM PrEP Guidelines Panel

The ASHM PrEP Guidelines Panel recommends that daily TD*/FTC should be recommended by clinicians as a crucial HIV-prevention strategy for all people who are at risk of HIV infection, that is, men who have sex with men (MSM), transgender people, heterosexual men and women, and people who inject drugs.

The ASHM PrEP Guidelines Panel endorses the recent recommendation by WHO that on-demand† PrEP should be offered as an alternative to daily PrEP for suitable patients.

(see Chapter 6 providing PrEP for more information on who is suitable for On-Demand† dosing).

† The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.

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2.
PrEP safety and efficacy

For a full review of PrEP safety and efficacy please see the CDC "Preexposure prophylaxis for the prevention of HIV infection in the United States -- 2021 update : a clinical practice guideline" https://stacks.cdc.gov/view/cdc/112360

3.
Indications for PrEP in Australia

HIV epidemiology

Australia has a concentrated human immunodeficiency virus (HIV) epidemic, whereupon in 2018 sexual contact between men accounted for approximately 70% of new HIV diagnoses **(1)**. During 2018, 23% of new diagnoses occurred in heterosexuals, and about one-third of these occurred where the person, or their partner came from a country with high HIV prevalence. Only 3% of new HIV diagnoses were attributable to injecting drug use alone.

Overall, the annual number of HIV diagnoses in Australia declined by 23% during 2014-2018 **(1)**, and this decrease was attributable to a 30% decline in notifications among men who have sex with men (MSM). There was no decline in HIV in Aboriginal and Torres Strait Islander people (hereafter referred to as Indigenous), in heterosexual people or in those born overseas.

In MSM, an 11% decline in HIV notifications was observed over five years between 2013 and 2017, but the decline increased to 15% in 2016-2017. However, this decline in HIV diagnoses among MSM was not uniform. In the last 10 years, notifications declined by 21% in Australian-born MSM, while the proportion of notifications almost doubled (from 28% to 52%) among overseas-born MSM **(1)**. The estimated proportion of undiagnosed HIV was also high among people born in Southeast Asia (27%) **(1)**. The uptake of HIV pre-exposure prophylaxis (PrEP) remained low in this population, comprising only 9% of PrEP participants in the EPIC NSW trial **(2)**. In Victoria, the incidence of HIV infection in newly arrived Asian-born MSM attending a sentinel sexual health clinic did not decline during 2013-2017 whereas the incidence fell by 45% in Australian-born MSM attending the same site **(3)**.

A 10% increase in HIV notifications of heterosexual exposure was reported between 2013 and 2017, with a 14% increase between 2016 and 2017, which was mainly attributed to the increase in the number of notifications among Australian-born men over these time periods (37% and 31%, respectively) **(1)**. In women, the notification rate remained stable during 2013-2017 (between 0.7 and 0.9 per 100,000), however, was low compared with that in men (0.9 vs 7.1 per 100,000 in 2017).

In the Indigenous population the rate of HIV notifications increased by 41% between 2013 and 2016, compared with a 12% decline in Australian-born non-Indigenous people, and in 2017 was 1.6 times higher than in the Australian-born non-Indigenous population **(1)**. During 2015–2017, more HIV notifications in the Indigenous population were attributed to heterosexual sex (21%) and injecting drug use (18%) than in the Australian-born non-Indigenous population (18% and 3%, respectively).

Among female sex workers, HIV incidence remained stable at or below 0.13 per 100 person-years during 2013–2017, and was 0.13 per 100 person-years in 2017 **(1)**. Similarly, for people who inject drugs (PWID), HIV prevalence has remained low in the past 10 years and ranged between 1.0% and 2.1% among people attending needle and syringe programs (2.1% in 2017), and 0.7% if gay and bisexual men were excluded from the sample. However, prevalence of HIV among Indigenous men in these programs has increased almost five times between 2010–2011 and 2016–2017 from 0.9% to 4.2% **(1)**.

HIV prevention

Overall, recent declines in HIV incidence and notifications concurred with Initiatives focused on improved uptake in HIV testing and treatment with simpler HIV treatment regimens. Consequently, 74% of people living with HIV in 2017 reached viral load suppression, thereby achieving zero risk of onward HIV transmission **(1)**.

By the end of 2018, 18,530 people, of whom 99% were male, were receiving Pharmaceutical Benefits Scheme (PBS)-subsidised PrEP in Australia **(4)**. Largely related to PrEP implementation, a 25% decline in new HIV diagnoses was observed among MSM in New South Wales, from 295 in the 12 months before the Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) study commenced to 221 in the 12 months following study commencement **(2)**.

As described above, HIV notifications in Indigenous populations increased by 41% between 2013 and 2016 and diverged from the trends in the Australian-born non-Indigenous population **(1)**. This divergence in HIV rates between the two populations possibly relates to a number of factors including a higher proportion of undiagnosed cases of HIV in the Indigenous population, sexual and drug-injecting practices and, importantly, a slower adoption of biomedical prevention strategies such as treatment as prevention and PrEP **(5)**. Hence intensive HIV prevention and treatment efforts, including the use of PrEP, are required to reverse this alarming trend **(6)**.

There are no available recent data about HIV testing uptake and access to antiretroviral drugs for PrEP for temporary residents who are ineligible to access Medicare (including short-term visitors, international students, skilled workers and some temporary residents awaiting decisions regarding their permanent residency as partners of citizens or permanent residents, asylum seekers and refugees).

In other population groups, harm reduction strategies for PWID and HIV and sexually transmissible infection (STI) prevention strategies for sex workers have been highly successful in keeping the prevalence and incidence of HIV at extremely low levels in Australia and among the lowest in the world. Current health promotion and HIV prevention strategies support PWID and sex workers to maintain these achievements, while access to PrEP may expand HIV prevention options **(7)**.

HIV risk categories and targeted availability of PrEP in Australia

Informed by the local epidemiology of HIV, access to PrEP in Australia has been pragmatically targeted to MSM at increased risk of HIV acquisition. Criteria for increased HIV risk were originally defined based on the evidence from the Sydney-based Health in Men (HIM) study **(8)**.

Table 3.1 summarises the main factors associated with an increased risk of HIV acquisition among gay and bisexual identified men in the Sydney-based HIM study **(8)**. Four factors were associated with HIV incidence of above 1.8 per 100 person-years; these factors formed the criteria for identifying people at high risk of HIV acquisition. Two more factors with an HIV incidence above 1.0 and below 1.8 per 100 person-years formed the criteria for identifying people at medium HIV acquisition risk. Although the HIM study collected data from 2001 to 2007 and HIV notification trends have changed since then, the same factors are likely to remain relevant to HIV transmission and its prevention today, and these factors were validated as eligibility criteria in an analysis of data from the Victorian PrEPX study **(9)** and continue to guide PrEP prescribing throughout Australia.

RISK FACTOR	HIV INCIDENCE PER 100 PERSON YEARS (95% CI)
All gay and bisexual men regardless of behavioural practices	0.78 (0.59–1.02)
A regular sexual partner of an HIV-positive man with whom condoms were not consistently used in the last 6 months	5.36 (2.78–10.25)
At least one episode of receptive, unprotected anal intercourse with any casual male partner with HIV infection or a male partner of unknown HIV status during the last 6 months	2.31 (1.48–3.63)
Rectal gonorrhoea diagnosis in last 6 months	7.01 (2.26–21.74)
Rectal chlamydia diagnosis in last 6 months	3.57 (1.34–9.52)
Methamphetamine use in last 6 months	1.89 (1.25–2.84)
More than one episode of anal intercourse during the last 3 months when proper condom use was not achieved (e.g. condoms slipped off or broke)	1.30 (0.95–1.77)
A regular sexual partner of CLAI or having at least one episode of insertive CLAI where the serostatus of partner is not known or is HIV positive	0.94 (0.35–2.52)
In uncircumcised men having at least one episode of insertive CLAI where the serostatus of partner is not known or is HIV positive	1.73 (0.43–6.90)
In circumcised men (comparison group, low risk, PrEP not recommended)	0.65 (0.16–2.61)

Table 3.1 Factors associated with elevated risk of HIV acquisition among men who have sex with men in the Health in Men (HIM) study, Australia, 2001–2007 **(8)**

Note that while the HIM study uses the terminology of 'gay and bisexual men', this guideline uses 'men who have sex with men' to focus on behaviour, rather than identity.

CI: confidence interval; CLAI: condomless anal intercourse; HIV: human immunodeficiency virus; PrEP: pre-exposure prophylaxis

Of note, due to the specifics of data collection for the HIM study, not all indicators were available to support each individual eligibility criterion for PrEP. Some indicators were collected in different forms, or had a different denominator or reference period. Most importantly, the HIV viral load of HIV-positive regular partners is now known to have a significant impact on HIV transmission **(10-12)**, and data on the HIV viral load of the source partners were not collected in the HIM study. Similarly, infectious syphilis was uncommon in the HIM cohort and was not associated with HIV transmission. However, its incidence has increased greatly since 2007 in Australia. Syphilis is associated with an increased risk of HIV among MSM globally **(13, 14)**, and is therefore included in the PrEP suitability assessment. Drug use is another important factor that influences sexual behaviour and HIV risk acquisition and that has emerged since the HIM study. Methamphetamine use has been associated with increased risk of HIV infection in high-income countries internationally **(15)**. In Australia associations have been observed between injecting drug use and sexual risk taking **(16)** with a higher incidence of drug use initiation occurring in younger versus older MSM **(17)**. Finally, the reference period

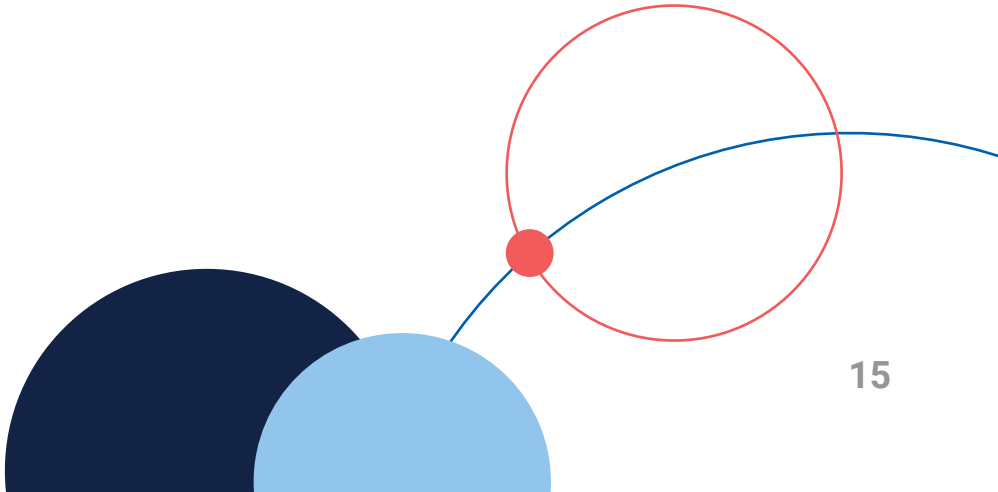
for PrEP suitability assessment is set up in these guidelines to reflect behaviour over the previous 3 months whereas the HIM study addressed behaviour over the previous 6 months **(8)**. In addition, the epidemiology of drug use has changed in MSM in Australia **(15-19)**.

The 2017 ASHM PrEP guidelines classified a person's risk of HIV acquisition as high or low based on criteria from the HIM study **(8)**. The 2017 guidelines recommended that an individual had to report HIV risk in the 3 months before commencing PrEP and that the individual anticipated that they would have HIV risk in the 3 months after commencing PrEP. Individual's risk of HIV acquisition were classified as high or low based on evidence from the HIM study **(8)**. Additionally, in the 2017 guidelines, clinicians were invited to consider offering PrEP on a case-by-case definition to people who did not meet high- or medium-risk criteria.

Importantly, since 2021, the ASHM PrEP guidelines no longer classify a person's risk of HIV acquisition as high or low and no longer require that an individual demonstrate HIV risk in the previous 3 months. Instead the current guidelines provide behavioural examples of what would make a person suitable for PrEP, including whether a person's quality of life would be likely to improve if they were offered PrEP, e.g. people with high levels of anxiety about HIV acquisition. (see **Suitability for PrEP**).

Overall, the epidemiological data highlight the need to strengthen the current strategies for HIV prevention especially in Indigenous populations, overseas-born MSM where HIV rates are rising and heterosexuals, which would include expanding and promoting the uptake of PrEP by all suitable people.

The PrEP suitability criteria that are provided in these guidelines are not intended to limit or deny access to PrEP to any person who seeks it. Instead, they are intended to help identify and actively recommend PrEP to people suitable for PrEP and to guide clinicians in their discussions about PrEP with patients who are uncertain about their HIV risk and need for PrEP use (see **Suitability for PrEP**).



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4.
Suitability for PrEP

Pre-exposure prophylaxis (PrEP) medications are registered in Australia with the Therapeutic Goods Administration (TGA) and they are subsidised by the Australian Pharmaceutical Benefits Scheme (PBS). All general practitioners, other medical specialists, and authorised nurse practitioners can prescribe PrEP using a PBS streamlined authority arrangement. No specialist training is required to prescribe PrEP, however resources and training guidance are available for clinicians who are new to prescribing PrEP.

People presenting for PrEP are typically at high risk of human immunodeficiency virus (HIV) infection and they should not be dissuaded from using PrEP. To do so is to deny a person access to one of the most effective HIV prevention tools currently available. Doctors and authorised nurse practitioners who are not comfortable prescribing PrEP should refer the patient immediately to a colleague, or another service that does provide PrEP.

It should also be highlighted that sexual history taking is a necessary and routine part of medical practice, and when this process identifies that a patient may be at risk of HIV, clinicians should proactively offer these patients PrEP. Furthermore clinicians are encouraged to raise PrEP as an HIV prevention strategy with patients whom they perceive to be at risk of HIV infection, even if the purpose of the patient's visit is not related to sexual health, sexually transmissible infections (STIs) or drug use.

These ASHM 2025 PrEP guidelines recommend daily PrEP for all people at risk of HIV infection. In addition, these guidelines also recommend that on-demand† PrEP should be offered as an alternative option to suitable patients. Please refer to section **providing PrEP** for further information on initiating PrEP.

PrEP providers need to obtain a thorough sexual and drug-use history at baseline to determine a person's suitability for PrEP and to review their ongoing need for PrEP at each 3-monthly clinical review. It is important to acknowledge that a person's behaviour may change over time, and that a person may wish to continue PrEP even if their current HIV acquisition risk is not high.

These guidelines acknowledge that PrEP should be recommended as an HIV prevention strategy for people who have been at risk of HIV infection during the previous 3 months and who foresee having similar risks in the next 3 months. These guidelines also recommend PrEP for people who have not been at risk of HIV infection during the previous 3 months, but whose circumstances have changed, and they foresee HIV risk occurring in the next 3 months.

Please note that people who are eligible for PrEP based on their sexual behaviour may be simultaneously eligible for PrEP based on their injecting and other drug use behaviour and vice versa.

The following suitability criteria can be used to help structure a discussion with a patient about their sexual health and behaviour. Guidance on how to initiate and guide a discussion about a person's sexual and drug using behaviour in primary practice is available (1).

Clinicians who have limited experience with prescribing PrEP are encouraged to discuss with a PrEP experienced clinician those patients whose PrEP suitability is unclear.

For clinicians who are skilled at and who prefer to evaluate people's PrEP suitability according to how the person reports their gender identity and sexuality, please refer to the alternative Suitability for PrEP chapter, Chapter 15.

PrEP suitability criteria for men who have sex with men

BOX 4.1 PREP SUITABILITY CRITERIA FOR MEN WHO HAVE SEX WITH MEN

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months:

- At least one episode of condomless anal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive condomless anal intercourse with any casual partner
- One or more episodes of engaging in sexualised drug use, sometimes referred to as 'chemsex'. In the Australian context this typically involves the use of crystal methamphetamine (Ice), but can also include the use of gamma hydroxybutyrate (GHB)
- One or more episodes of rectal gonorrhoea, rectal chlamydia or infectious syphilis, including any STIs diagnosed at screening for PrEP
- More than one episode of anal intercourse where a condom slipped off or broke where the HIV serostatus of the partner was not known, or where the partner was HIV positive and not on treatment or had a detectable viral load on treatment.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months.

Note: The following list is not exhaustive and there are likely to be many other scenarios where PrEP could be suitably offered for people whose HIV risk acquisition is exclusively in the future:

- When a person plans to travel during which time they anticipate that they will be having condomless sex with casual partners
- When a person plans to return home to an overseas country which has a high HIV prevalence during which time they anticipate that they will be having condomless sex with casual partners
- When a person reports that they have recently left a monogamous relationship and will be having condomless sex with casual partners in the future
- When a person reports that they will be entering or leaving institutional or correctional facilities in the near future where they may have condomless sex with casual partners in the future
- When a person presents with concerns of deteriorating mental health and a history of having previously increased their HIV acquisition risk behaviour in this setting
- When a person presents with a history of intermittent binge drinking of alcohol or recreational drug use and a history of having had increased their HIV acquisition risk behaviour in this setting.

The clinician should consider prescribing PrEP also in the following circumstances:

- When an HIV serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment
- When a person reports being so anxious about HIV infection that it may prevent them from having regular HIV testing, or engaging in any form of anal sex
- When a person presents with a history of recurrent genital ulceration or dermatoses (e.g. psoriasis), as this may increase the risk of HIV transmission.

PrEP suitability criteria for trans and gender diverse people

Only a small proportion of participants in PrEP studies have been transgender (trans) or gender diverse people (2, 3, 4). As a result, limited data are available for these populations. Incorrect assumptions can be made about trans people and their sexual practices, as they may practice vaginal/neovaginal and anal intercourse, both insertive and receptive. Trans and gender-diverse people who are at risk of acquiring HIV on the basis of their sexual history are eligible to access PrEP. It is essential for clinicians to take a sexual history using appropriate and sensitive language to assess risk.

BOX 4.2 PREP SUITABILITY CRITERIA FOR TRANS AND GENDER DIVERSE PEOPLE

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months:

- At least one episode of condomless anal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive condomless anal intercourse with any with any casual partner of unknown status
- More than one episode of anal or vaginal intercourse where a condom slipped off or broke where the HIV serostatus of the partner was not known, or where the partner was HIV positive and not on treatment or had a detectable viral load on treatment
- One or more episodes of engaging in sexualised drug use, sometimes referred to as 'chemsex'. In the Australian context this typically involves the use of crystal methamphetamine (Ice) but can also include the use of gamma hydroxybutyrate (GHB)
- One or more episodes of rectal gonorrhoea, rectal chlamydia or infectious syphilis including any STIs diagnosed at screening for PrEP.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months:

- When a person plans to travel during which time they anticipate that they will be having condomless sex with casual partners
- When a person plans to return home to an overseas country which has a high HIV prevalence during which time they anticipate that they will be having condomless sex with casual partners
- When a person reports that they have recently left a monogamous relationship and will be having condomless sex with casual partners in the future
- When a person reports that they will be entering or leaving institutional or correctional facilities in the near future where they may have condomless sex with casual partners in the future
- When a person presents with concerns of deteriorating mental health and a history of having previously increased their HIV acquisition risk behaviour in this setting
- When a person presents with a history of intermittent binge drinking of alcohol or recreational drug use and a history of having had increased their HIV acquisition risk behaviour in this setting.

The clinician should consider prescribing PrEP also in the following circumstances:

- When an HIV serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment
- When a person reports being so anxious about HIV infection that it may prevent them from having regular HIV testing or engaging in any form of anal or vaginal sex
- When a person presents with a history of recurrent genital ulceration or dermatoses (e.g.psoriasis), as this increases the potential risk of HIV transmission.

PrEP suitability criteria for heterosexuals

BOX 4.3 PREP SUITABILITY CRITERIA FOR HETEROSEXUALS

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months

- At least one episode of condomless anal or vaginal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive anal or vaginal condomless intercourse with any casual HIV-positive partner or a male partner of unknown status
- Episodes of planned condomless insertive or receptive vaginal sex in an effort to conceive with an HIV-positive partner, regardless of the HIV-positive partner's viral load.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months:

- Future episodes of planned condomless insertive or receptive vaginal sex in an effort to conceive with an HIV-positive partner, regardless of the HIV-positive partner's viral load
- When a person plans to travel to countries with high HIV prevalence during which time they anticipate having condomless sex with casual partners who are HIV positive or of unknown HIV serostatus
- When a person plans to return home to an overseas country which has a high HIV prevalence during which time they anticipate that they will be having condomless sex with casual partners
- When a person reports that they have recently left a monogamous relationship and will be having condomless sex with a casual HIV-positive partner, or a male or female partner of unknown HIV serostatus from a country with high HIV prevalence, or a male partner who is thought to have sex with men
- When a person presents with concerns of deteriorating mental health and a history of having had increased their HIV acquisition risk behaviour in this setting
- When a person presents with a history of intermittent binge drinking of alcohol or recreational drug use and a history of having had increased their HIV acquisition risk behaviour in this setting.

The clinician should consider prescribing PrEP also in the following circumstances:

- When an HIV serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment.

PrEP suitability criteria for people who inject drugs

In the first instance, people who inject drugs (PWID) should be advised of and provided with options for using sterile needles, syringes and other injecting equipment, and offered opioid substitution therapy for those who use opioids. People who inject drugs can be referred to local needle and syringe programs, or the Australian Injecting and Illicit Drug Users League affiliates in their state or territory.

Because PWID are susceptible to a range of infections and injuries, PrEP and other HIV-prevention interventions should be integrated into prevention and clinical care services for hepatitis A, B and C infection

and other infectious diseases, and overdose prevention. These interventions include screening for hepatitis A, B and C viruses and providing incentivised vaccination for hepatitis A and B where clinically indicated, as well as screening for injection-related injuries and infections including abscesses, septicaemia and endocarditis **(5)**.

The ASHM PrEP Guidelines Panel is cognisant of the concerns of the International Network of People who Use Drugs. The Network cautions against prioritising PrEP at the expense of other proven interventions as the prime HIV-prevention strategy for people who inject drugs, and emphasises that access to harm reduction services remains a critical component of HIV prevention in people who inject drugs **(6)**. This approach is particularly relevant in Australia where sterile needle and syringe coverage is high and HIV prevalence and incidence among people who inject drugs remains low and stable **(7, 8)**.

A recent systematic review of HIV-treatment adherence among PWID in the United States and Canada, undertaken to inform potential PrEP adherence interventions for people who inject drugs, found that younger age, female sex, homelessness and incarceration were obstacles to HIV treatment adherence **(9)**. By comparison, self-sufficiency, use of opioid substitution therapy, and high quality patient-provider relationships were facilitators for adherence **(9)**. Self-reports from HIV-negative people who inject drugs were that HIV–related stigma in social networks, negative experiences with health-care providers, lack of money, homelessness and the criminal justice system were likely barriers to PrEP access **(10)**. These factors should be considered when providing support to people commencing PrEP when they are at risk of HIV through injecting drug use.

The ASHM PrEP Guidelines Panel will continue to monitor the outcomes of the few ongoing studies of HIV PrEP in PWID.

BOX 4.4 PREP SUITABILITY CRITERIA FOR PEOPLE WHO INJECT DRUGS

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months:

- Shared injecting equipment with an HIV-positive person or with a gay or bisexual man of unknown HIV status
- At least one episode of condomless anal or vaginal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive anal or vaginal condomless intercourse with any casual HIV-positive partner or a male homosexual or bisexual partner of unknown status.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months.

- A person has recently (re)commenced injecting drugs and is injecting with a person who is HIV positive, or with a gay or bisexual man whose HIV status is unknown
- When a person plans to travel to countries with high HIV prevalence during which time they anticipate injecting drugs with other people who are HIV positive or of unknown HIV serostatus.
- When a person reports that they will be entering, or leaving institutional or correctional facilities in the near future during which time they may inject drugs with people who are HIV positive or of unknown HIV serostatus

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5.
Clinical assessment before starting PrEP

All patients whose sexual or drug injection history indicates the recommendation or consideration of pre-exposure prophylaxis (PrEP), and who are interested in taking PrEP, must undergo laboratory testing. The tests identify those for whom this intervention would be harmful, or in whom it could present specific health risks that would require close monitoring.

HIV testing

For patients' safety, those with acute or chronic human immunodeficiency virus (HIV) infection should be identified through taking a medical history and HIV testing. A negative HIV test result must be documented at the time the patient is evaluated for PrEP as the daily, or on-demand† tenofovir disoproxil* and emtricitabine (TD*/FTC) combination alone is insufficient for treatment of acute or chronic HIV infection.

HIV testing must be repeated every 3 months when patients attend for a prescription refill. This requirement for quarterly visits should be explained to patients during the initial discussion about whether PrEP is appropriate for them.

A fourth-generation HIV antibody/antigen venous blood test should be used and should be performed within 7 days of the patient being evaluated for PrEP. Clinicians should tell patients to start PrEP within 7 days of the day that their HIV-negative test was performed.

Rapid, point-of-care tests (PoCT) should not be used alone to screen for HIV infection when considering PrEP because they are less sensitive than blood tests. Failure to detect very early HIV infection by rapid testing in the PrEP context has been reported (1). This includes the Atomo HIV Self-Test, a rapid home-based HIV testing kit which was approved for online purchase in Australia by the TGA in November 2018. However, a rapid PoCT can be used for the same day initiation of PrEP providing that a venous blood test for a fourth generation HIV antibody/ antigen test is obtained and tested simultaneously. A PoCT can exclude potential PrEP users who are found to be HIV positive, and any reactive PoCT should be confirmed by conventional laboratory testing in line with the **Australian HIV Testing Policy**. Clinicians should not accept patient-reported HIV test results, including home-based HIV test results, or documented anonymous test results. Any positive HIV antibody test result must be managed according to the Australian HIV Testing Policy and local management guidelines (**www.testingportal.ashm.org.au**).

A course of non-occupational post-exposure prophylaxis (nPEP) may be required before transitioning to PrEP, in accordance with the PEP and nPEP guidelines **(2)** if a patient has had a recent high-risk exposure (within 72 hours). See the **PEP guidelines** for more information.

Patients who have had a recent high-risk exposure outside the 72 hour window for the commencement of nPEP should be started on PrEP and closely monitored for seroconversion using a fourth-generation HIV test for the next 2–8 weeks before reverting to standard PrEP monitoring. HIV viral load and HIV proviral DNA tests are not recommended to screen for early HIV infection. These tests are not reimbursed by Medicare and may take 10-14 days for results to be available.

Acute HIV infection should be suspected in individuals at high risk of HIV who may have had recent exposure to HIV (e.g. no condom or a condom broke during sex with an HIV-positive partner not on treatment, or casual partner of MSM; recent injecting drug use with shared injection equipment with MSM, or person known to be HIV positive).

In a prospective study of 2,226 people at high risk of HIV infection who underwent twice-weekly HIV nucleic acid testing, 50 people were evaluated for their clinical signs and symptoms during acute HIV infection. Symptoms and signs occurred in 94% of participants with acute HIV infection, just before and around the time of peak HIV viraemia **(3)**. The most common symptoms were fever, headache and malaise, while the most common signs were related to the head, eyes, ears, nose, throat, tachycardia and lymphadenopathy (Table 5.1).

	AFRICA (N=31)		THAILAND (N=17)		OVERALL (N=48)	
	n	%	n	%	n	%
SYMPTOM						
Fever	18	55	7	41	25	50
Headache	17	52	6	35	23	46
Feeling of illness	14	42	5	29	19	38
Coughing	10	30	9	53.5	19	38
ABNORMALITY						
HEENT [a]	6	18	16	94	22	44
Lymphadenopathy [b]	9	9	16	94	19	38
Tachycardia	11	33	5	29	16	32

Table 5.1 Symptoms and abnormalities associated with primary or acute HIV infection, overall and by region **(3)**.

[a] Head, ears, eyes, nose and throat.

[b] A condition or disease affecting the lymph glands of the body resulting in lymph nodes that are abnormal in size, consistency or number.

Initiation of TD*/FTC PrEP in individuals with undiagnosed primary or acute (symptomatic) HIV infection has been associated with the development of resistance to TD*/FTC, mostly commonly to the FTC component **(4-7)**.

People who present with signs or symptoms consistent with acute HIV infection should not be commenced on PrEP until HIV infection has been excluded.

Patients with indeterminate HIV test results at baseline should not be started on PrEP. They should be assessed for early HIV infection and treated according to local antiretroviral treatment guidelines **(8)**. Such patients can only be started on PrEP if and when HIV infection is excluded.

Concerns about TD* or FTC resistance

Overall, the risk of developing TD* or FTC resistance among participants on PrEP is low **(9)**. According to a World Health Organization (WHO) meta-analysis of HIV resistance data from randomised clinical trials of PrEP, participants on PrEP versus placebo who started PrEP at the time of acute HIV infection had a higher risk of developing resistance, with more cases of resistance developing to FTC than to TD*. Only a few TD* or FTC mutations were recorded among participants who seroconverted after randomisation into clinical trials **(9)**. Similar findings were reported in a more recent review of clinical trials and case reports of HIV resistance occurring in the PrEP setting **(10)**. Mathematical modelling shows that the number of HIV-1 infections that would be averted by PrEP greatly exceeds the number of drug-resistant infections that could occur **(11)**.

Assessment of renal function at baseline

In HIV-positive patients, the use of tenofovir was reviewed in a meta-analysis and was associated with a statistically significant loss of renal function, with the effect being judged as clinically modest **(12)**. Tenofovir use was not associated with increased risk of fractures, hypophosphataemia or severe proteinuria **(12)**. Rarely, proximal renal tubular dysfunction (including Fanconi syndrome) may occur with TD* use **(12-14)**.

Overall, tenofovir use in PrEP studies has not been associated with significant clinical renal problems (15-17). The Iniciativa Profilaxis Pre-Exposición (iPrEX) study showed a small but statistically significant mean decline in creatinine clearance (CrCL) from baseline but the decline in CrCL was reversible upon PrEP cessation **(15)**. Factors associated with a decline in estimated Glomerular Filtration Rate (eGFR) include commencement of PrEP at age 40 years or over, a baseline eGFR below 90 mL/min/1.73m^2, and good adherence **(17)**. **There is no data for people using PrEP who have an eGFR below 60 mL/min/1.73m^2 therefore starting PrEP in individuals whose eGFR is well established to be below 60 mL/min/1.73m^2 is not recommended.** However, see comments below on managing individuals who are found to newly have an eGFR around 60 mL/min/1.73m^2 at baseline testing.

Data from the iPrEx open-label extension (iPrEX-OLE) study found a significant increase in both urine alpha1 microglobulin, a urine marker of impaired tubular reabsorption, and proteinuria after 6 months of TDF/FTC exposure suggesting that subclinical tubular injury occurs on PrEP **(18)**.

There are limited data regarding whether on-demand† versus daily PrEP reduces the likelihood of renal toxicity. However, in the Intervention Préventive de l'Exposition aux Risques avec et pour les Gays (IPERGAY) study, no significant decline was observed in the mean slope of eGFR in the tenofovir and emtricitabine versus placebo arms over a median of 9.3 months follow-up **(19)**, suggesting that on-demand† PrEP may not influence renal function. In the ADAPT study, a creatinine elevation was observed in 9% of 178 participants evaluated, but creatinine elevation did not differ between participants in the daily, time-driven and on-demand PrEP study arms (P = 0.05) **(20)**.

Recent data from the DISCOVER study where MSM and transgender women at risk of HIV were randomised to TDF/FTC versus tenofovir alafenamide (TAF)/FTC reported a significant difference in change in eGFR and tubular proteins during the study favouring TAF/FTC **(21)**. More broadly the DISCOVER study found that TAF/FTC was non-inferior to TDF/FTC in terms of preventing HIV infection **(21)**, however TAF/FTC has not been licensed yet in Australia for use as PrEP.

For all patients considered for PrEP, their risk factors for chronic kidney disease (CKD) should be assessed at baseline. These risk factors include diabetes, hypertension, smoking, concurrent medications and a known history of renal impairment or history of kidney injury or structural abnormality and Aboriginal and Torres Strait Islander status. Measurements of baseline serum creatinine, eGFR, the urine protein: creatinine ratio (PCR) and blood pressure should also be taken. The Cockcroft–Gault formula for estimating creatinine clearance (CrCl) (see Appendix 2) is regarded as the ideal way to measure the eGFR. However, for most practitioners, this is not practical. Instead, it is reasonable to measure the patient's renal function using the eGFR as reported by the laboratories.

For individuals who are found to newly have an eGFR around 60 mL/min/1.73m^2 at baseline, the eGFR should be repeated within 7 days because clinical situations occur when the eGFR may be unreliable, e.g. recent consumption of cooked meat. In this setting the clinician should ask the individual to fast or avoid a cooked meat meal within 4 hours of repeat eGFR testing. Exceptional dietary intake e.g. vegetarian diet, high protein diet, creatine supplements, and extremes of body size (e.g. high muscle mass) may underestimate eGFR. Being underweight or having low muscle mass may overestimate eGFR.

If after repeat testing an individual's eGFR remains just below or just above 60 mL/min/1.73m^2, it is recommended that the clinician speak to a specialist in PrEP as these patients may still be able to commence PrEP with close monitoring. Of note, in this setting on-demand† PrEP may be a suitable option if the patient is **suitable**.

These guidelines recommend that creatinine, eGFR and urinary PCR measurements for each person are evaluated at baseline. The eGFR should be repeated 3 months after commencing PrEP then 6 monthly thereafter. However, based on currently available evidence, more intensive monitoring may be warranted in the following individuals:

- those over the age of 40 years
- those with a baseline eGFR of less than 90 mL/min/1.73 m^2
- those with other comorbidities (e.g. hypertension, diabetes)
- those taking nephrotoxic drugs.

A minority of individuals may experience a decline in eGFR; the Australian CKD Management in General Practice recommends further investigations and consideration of a referral to a specialist renal service when there is sustained decrease in eGFR of 25% or more or a sustained decrease in eGFR of 15 mL/min/ 1.73 m^2 **(22)**.

Assessment and management of sexually transmissible infections at baseline

Individuals at risk for HIV infection are also at high risk for STIs. Clinicians should screen for STIs (specifically gonorrhoea, chlamydia and infectious syphilis) using the standard-of-care tests and procedures, and manage any detected STI as recommended by the Australian STI Management Guidelines **(23)**. Importantly the presence of an STI at baseline should not delay the commencement of PrEP. Of note, in the PrEPX study it was reported that 10.2% of 1,774 evaluable study participants tested positive for STIs at baseline **(24)**.

Patients starting on PrEP should be informed about:

- prevention of STI acquisition and transmission
- frequency of STI testing
- signs and symptoms of STIs.

Patients should be encouraged to present for testing and treatment whenever signs or symptoms of STIs appear.

Assessment of hepatitis A, B and C status

Patients being suitable for PrEP can also be at risk of acquiring hepatitis A, hepatitis B virus (HBV) infection **(25)** and hepatitis C virus (HCV) infection **(26)**. Hepatitis A, HBV and HCV infection status should be documented by screening serology when PrEP is initiated.

Vaccination against hepatitis A and HBV is recommended for all susceptible priority populations, which include MSM, sex workers, people from countries with a high HIV, HBV or HCV prevalence, and their sexual partners and people who inject drugs (27, 28). Individuals identified at baseline as having undiagnosed chronic hepatitis B should be referred to a clinician experienced in the management of hepatitis B for treatment assessment. Individuals with chronic hepatitis B infection may be offered daily PrEP but may only be offered on-demand† PrEP if they meet certain criteria (see **Chapter 9 - Special Clinical Considerations**). They should also be counselled on the importance of strict adherence to PrEP to prevent both a flare in their hepatitis B infection and the development of hepatitis B resistance to TD*/FTC. Individuals identified at baseline with undiagnosed hepatitis C infection should be referred to a clinician experienced in hepatitis C management for consideration of hepatitis C treatment. A diagnosis of hepatitis B or hepatitis C is not an obstacle to HIV PrEP initiation.

Assessment of bone health

Low bone mineral density (BMD) was observed at baseline in approximately 10% of individuals receiving TD*/FTC for PrEP in the IPREX study **(29)**. Individuals should be counselled about the effects of TD* on BMD and counselled to decrease alcohol and cigarette use, to undertake weight-bearing exercise and ensure their diet provides adequate amounts of calcium and vitamin D **(30)**. A clinician may suspect that an individual is vitamin D deficient and may wish to test their vitamin D levels. There is no evidence that over-the-counter vitamin D supplements reduce tenofovir-related BMD changes.

A small but statistically significant decline in BMD was observed by week 24 in participants of the iPrEX study. The decline in BMD correlated directly with levels of intracellular TD*-DP and was found to be reversible once PrEP was ceased **(31)**.

There are no data available on whether on-demand† PrEP is less likely to cause a decline in BMD.

Recent data from the DISCOVER study, found that TAF/FTC versus TDF/FTC was associated with less decline in BMD **(21)**.

A person with a history of osteoporosis will require careful monitoring while on PrEP. If the clinician suspects that a person may have osteoporosis, they may recommend BMD testing. BMD testing is rebated in Australia under specific clinical circumstances; Information about BMD rebates can be found on the Australian Government's DoHDA website. In those people over the age of 40 years thought to be at risk of having reduced BMD, a FRAX® tool to evaluate fracture risk can be used to assess the need for dual-energy X-ray absorptiometry (DXA) scanning. For further information see **https://www.sheffield.ac.uk/FRAX/tool.aspx?country=31**.

Assessment for pregnancy in women of childbearing age

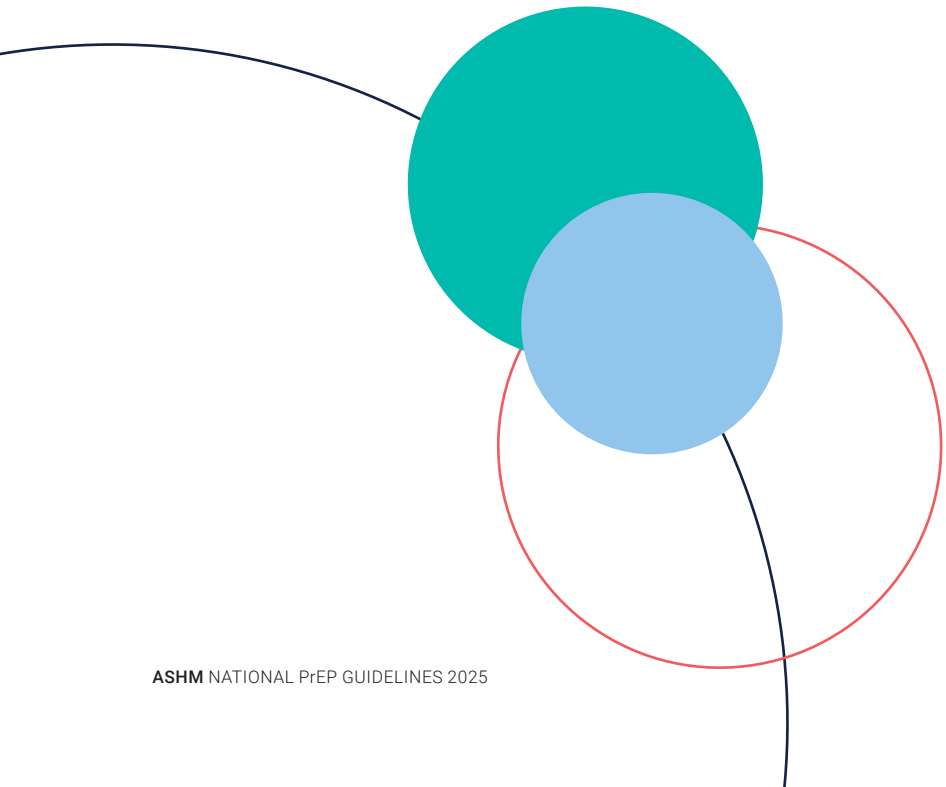
The risk of HIV transmission to women increases by over two-fold when they are pregnant **(32)**. As reviewed recently, current evidence suggests that PrEP can be used safely during pregnancy and breastfeeding **(33)**.

The use of TD*-containing regimens by HIV positive women throughout pregnancy has not been associated with adverse pregnancy outcomes, but lowered BMD has been observed in newborns exposed to TD* in utero (34, 35) as has a lower length and head circumference at 1 year of age **(35)**.

In the Partners PrEP study, which compared the efficacy of TDF/FTC versus TDF versus placebo to reduce HIV transmission in African heterosexual HIV-serodifferent couples, 431 pregnancies occurred; the average duration of in utero PrEP exposure was 5 weeks. There was no difference in the incidence of pregnancy, birth outcomes or infant growth in women who received TDF or TDF/FTC versus placebo PrEP **(36)**. However, as noted by the authors, the confidence intervals for these findings were wide and therefore definitive statements about the safety of TDF/FTC as PrEP during pregnancy could not be made based on this study's findings. A subsequent study from this group examined the pregnancy outcomes of 30 women who continued to use PrEP during pregnancy compared to 96 pregnancies without PrEP exposure. The authors found that there was no increase in adverse pregnancy outcomes or restrictions in infant growth between the two groups **(37)**. The World Health Organization has included PrEP as an HIV prevention strategy during pregnancy **(38)** and a number of other jurisdictions recommend PrEP for safe conception and for use during pregnancy and breastfeeding **(39)**.

Some women with an HIV-positive partner may prefer to continue PrEP while pregnant, due to an increased risk of acquisition of HIV if their partner is not reliably virologically supressed during pregnancy **(39)**. The lead in time for PrEP to reach highly effective levels in women is 7 days **(40)**. A study evaluating antiretroviral excretion in breast milk and infant absorption suggests PrEP can be safely used during breastfeeding with minimal infant drug exposure **(41)**.

The ASHM PrEP Guidelines Panel will continue to monitor the safety of TD*/FTC PrEP regimens when used during pregnancy and breastfeeding.



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6.
Providing Oral PrEP

Goals of PrEP

The ultimate goal of HIV pre-exposure prophylaxis (PrEP) is to reduce the acquisition of HIV infection and its resultant morbidity, mortality and associated cost to individuals and society. Therefore, clinicians initiating the provision of PrEP should:

- prescribe medication regimens that are proven safe and effective for HIV-negative people who are suitable for PrEP to reduce their risk of HIV acquisition. Only co-formulated tenofovir and emtricitabine (TD*/FTC) is licensed in Australia for use as PrEP and is the only regimen that should be used.
- educate patients about the medications and the dosing regimen (daily for all patients, or on-demand† for suitable patients, to optimise safe medication use.
- provide counselling on sexually transmissible infections (STIs) and their prevention.
- provide medication-adherence support and counselling to help patients achieve and maintain protective levels of medication.
- provide HIV risk-reduction support and offer harm reduction including referrals to help patients minimise their risk of acquiring HIV, viral hepatitis B and C and STIs.
- provide effective contraception to women who are taking PrEP and who do not wish to become pregnant.
- monitor patients on a quarterly basis to screen for HIV infection, STIs and toxicity and to determine whether PrEP remains indicated.

PrEP licensing in Australia

Co-formulated TD*/FTC is registered by the Therapeutic Goods Administration (TGA) for daily use and is subsidised by the Pharmaceutical Benefits Scheme (PBS) in Australia.

Daily PrEP

Daily PrEP is the most commonly prescribed PrEP regimen in Australia. Daily use of TD*/FTC is highly efficacious at preventing HIV transmission in MSM **(1, 2)**, heterosexuals **(3)**, transgender women **(4)** and people who inject drugs (PWID) **(5)** in the setting of high medication adherence. A detailed review of these and other studies that have demonstrated the efficacy and effectiveness of daily PrEP is beyond the scope of these guidelines. For more information see **PrEP efficacy**.

The ASHM PrEP Guidelines Panel continues to recommend that daily TD*/FTC should be offered to all populations at risk of HIV infection.

* The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.

Figure 6.1 Daily PrEP

On-demand† PrEP

On-demand† PrEP involves taking two tablets of TD*/FTC 2–24 hours before a potential sexual exposure to HIV, followed by a third tablet 24 hours after the first dose and a fourth tablet 48 hours after the first dose. If sex continues beyond one day, a user of on-demand† PrEP can stay protected by continuing to take a pill every 24 hours for each day that sex occurs. A PrEP pill should be taken each day for the two days following the last day that sex occurred.

Please note: the Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.

Figure 6.2 On-Demand† PrEP

† The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.

On-demand PrEP (also known as "event-based" or "event-driven" PrEP) is as effective as daily PrEP in preventing HIV transmission **(1)**. The World Health Organization (WHO) now recommends the use of on-demand PrEP as an option to prevent sexual transmission of HIV for:

- **Cisgender men, regardless of the sex of their sexual partners.**
- **Trans and gender diverse people who were assigned the male sex at birth, who are not taking exogenous oestradiol-based hormones.** Small studies have indicated that the use of gender-affirming oestrogen may reduce the concentrations of TDF and FTC among transgender women by 12–27%, **(3, 4)** potentially undermining the effectiveness of on-demand PrEP.

The ASHM PrEP Guidelines Panel endorses these WHO recommendations.

These recommendations apply only to scenarios in which the risk of HIV transmission arises from sexual exposure, not exposure through intravenous drug use. The ASHM PrEP Guidelines Panel recommends that caution be used in recommending on-demand PrEP to adolescent MSM because there have been no trials of on-demand PrEP in adolescent MSM and because adherence rates to daily PrEP have been consistently low in studies of adolescent MSM **(7, 8)**.

Whereas on-demand† PrEP was previously contraindicated in people living with chronic hepatitis B infection, on-demand PrEP may now be considered for this patient group (see section on **hepatitis B and PrEP**).

Evidence in support of on-demand† PrEP dosing

Data on the efficacy of non-daily PrEP dosing are available for cis-gender MSM. Very few transgender women have been evaluated in randomised controlled trials of on-demand† PrEP **(9-11)**; nor have such trials been undertaken in cis-gender women or cis-or transgender men, or in people whose principal HIV exposure risk is injecting drug use. Pharmacological studies in cis-gender women suggest that on-demand† PrEP does not provide adequate tissue levels of PrEP to provide high levels of HIV protection and on-demand† PrEP should not be recommended for cis-gender women.

Data on how efficacious on-demand† PrEP is for MSM in reducing HIV transmission came initially from the randomised, placebo-controlled trial, IPERGAY (Intervention Préventive de l'Exposition aux Risques avec et pour les Gays) **(12)**. This study evaluated the efficacy of on-demand† PrEP comprising two tablets of TDF/FTC (versus placebo) taken 2–24 hours before potential sexual exposure to HIV, followed by a third tablet 24 hours after the first dose and a fourth tablet 48 hours after the first dose. If multiple episodes of sex occurred, the participants were advised to continue to take one tablet daily until the last sex act then take the two final doses, 24 hours apart. If sexual activity was resumed within a week, a single, rather than a double dose before sex was recommended. If sexual activity resumed more than a week later, the loading dose schedule (two tablets) was recommenced. The incidence of HIV was high in the placebo group (6.6 per 100 person-years) and a risk reduction in the TDF-FTC group of 86% [95% confidence interval (CI), 40 to 98; p = 0.002] was observed **(12)**.

Demonstration studies have been undertaken to determine how effective on-demand† PrEP is when used in community settings. In an open-label extension study of the IPERGAY study, an HIV risk reduction of 97% (95% CI, 81–100) with on-demand† PrEP was reported in 361 participants with a median follow-up of 18 months **(10)**. In a study of 1,069 people commencing PrEP in a single clinic in France, four HIV infections were diagnosed over 486 years of person follow-up **(9)**. In the French Prévenir study, an interim analysis presented in July 2019 at the IAS conference on HIV science showed that of 2,143 participants, 47% took daily PrEP and

52% took on-demand† PrEP **(11)**. The median number of partners in the 3 months before PrEP commencement was 15 (IQR: 7-25) in the daily group and 10 (IQR 5-15) in the on-demand† group (p < 0.001). The median number of condomless sex events in the previous 4 weeks was 2 (0 to 8) and 2 (0 to 4), in the daily and on-demand† participants, respectively (p = 0.04). Follow-up in the daily and on-demand† groups was 744 and 830 person-years, respectively. The HIV-1 incidence was 0 (95% CI: 0-0.5) and 0 (95% CI: 0-0.4) per 100 person-years in the daily and on-demand† groups, respectively **(11)**.

† The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.

The efficacy of on-demand† PrEP in people who use it infrequently

To address the question of whether on-demand† PrEP is efficacious for people using it infrequently, the IPERGAY study team undertook a post-hoc analysis of IPERGAY study participants who reported relatively infrequent sex **(13)**. Overall, IPERGAY participants reported using a median of 15 PrEP tablets per month (interquartile range (IQR 9–21). The post-hoc study looked at the follow-up time between two consecutive visits during which participants in the placebo and active study arms used ≤ 15 tablets per month and reported they used PrEP 'systematically or often' and not 'from time to time or never". During these periods of lower PrEP use, participants had a median of five episodes of sex per month (IQR 2-10) and used a median of 9.5 tablets per month (IQR 6-13). Six HIV infections occurred in the placebo arm (incidence: 9.3 per 100 person-years, total follow-up time: 64.8 person-years) and 0 in the TDF/FTC arm (incidence: 0 per 100 person-years, total follow-up time: 68.9 person years, p = 0.013). The relative reduction of HIV incidence in the treatment group was 100% (95% CI, 20-100). The study investigators concluded that an on-demand† PrEP strategy remains highly effective in MSM even when they have infrequent sex **(13)**. Notably, of concern to the ASHM PrEP Guidelines Panel were the wide 95% confidence intervals of the relative risk reduction in this group of IPERGAY participants practicing infrequent sex. However, the recently updated data from the Prévenir study **(11)** are reassuring in terms of the efficacy of less frequent use of on-demand† PrEP. These updated data show that the median number of partners in the previous 3 months for participants using on-demand† PrEP was 10 (IQR 5-15) and the median number of condomless sex events in the previous 4 weeks was 2 (0 to 4) (p = 0.04) with an associated HIV incidence in the on-demand† participants of 0 (95% CI: 0-0.4) **(11)**.

Toxicity and on-demand† PrEP

There are few data available to determine whether on-demand† PrEP offers less toxicity. In the IPERGAY study, no significant decline in the mean slope of estimated glomerular filtration rate (eGFR) in the TD*/FTC versus placebo arms was observed over a median of 9.3 months follow-up **(14)**. In the HIV Prevention Trials Network (HPTN) study 067, the Alternative Dosing to Augment PrEP Pill Taking (ADAPT) study, 9% of 178 participants at one study site had creatinine elevation, but this was not significantly different between participants in the daily, time-driven and on-demand† PrEP study arms (p = 0.05) **(15)**.

Preference for on-demand† versus daily PrEP

In the ongoing French Prévenir study, in which MSM are offered the choice of daily or on-demand† PrEP, approximately half of the participants opt for each regimen **(11)**. In the AM PrEP (the Netherlands) and Be PrEPared (Belgium) implementation studies, approximately one-third of men opted to take PrEP on-demand† **(16)**. In a report from the PRELUDE study from New South Wales, one third of participants enrolling in the study expressed a preference for non-daily PrEP **(17)**. Recent data from previous participants of the Victorian PrEPX study showed that 48% would be interested in participating in an on-demand† PrEP study **(18)** and this interest was most strongly associated with having sex infrequently and concerns about long-term toxicity **(18)**.

The choice of PrEP schedule: daily versus on-demand† PrEP

Daily PrEP is suitable for all people who are at risk of HIV. Daily PrEP is the only PrEP regimen that is recommended for cisgender women, transgender women on exogenous oestrogen therapy, transgender men who have vaginal sex, and for people who inject drugs (PWID) **(6)**.

The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia but may be suitable for certain populations as an off label indication.

On-demand† PrEP would be suitable for those PrEP users whose preference is for the on-demand regimen, who have sex less than twice a week, and who can plan for sex at least 2 hours in advance. Other reasons that PrEP users may choose or merit on-demand† PrEP include side-effects from daily PrEP, impaired kidney function or financial constraints.

The ASHM PrEP Guidelines Panel will continue to monitor HIV incidence in MSM using on-demand† PrEP, including those who use on-demand† PrEP less than fortnightly **(11)**.

Summary of when to recommend daily and on-demand† PrEP

Based on the evidence, the ASHM PrEP Guidelines Panel continues to recommend daily TD*/FTC dosing for all populations suitable for PrEP. The ASHM PrEP Guidelines Panel recommends that on-demand† PrEP should be offered to cisgender men regardless of the sex of their sexual partners. On-demand† PrEP is also recommended for trans and gender diverse people assigned male at birth who are not taking oestradiol-based hormone therapy.

For those suitable for on-demand† PrEP, on-demand† PrEP should be offered when this preference is expressed, when the person has at-risk sex less than twice a week, when the at-risk sex is unpredictable, and when sex can be delayed for 2 hours.

Other PrEP dosing schedules

There is some online guidance currently available that recommends that MSM taking PrEP can use a dosing schedule where they take a single dose of PrEP on Tuesdays, Thursdays, Saturdays and Sundays, known as 'the Ts and Ss'. While the motive for simplifying the PrEP dosing schedule is laudable the ASHM PrEP Guidelines Panel does not recommend the 'Ts and Ss' dosing schedule as it has not been tested in a clinical trial to demonstrate its efficacy in preventing HIV transmission.

Evaluation of the need for ongoing PrEP

Along with encouraging safer sex practices and safer injecting techniques, as needed, clinicians should support their patients to decide when to commence PrEP and when to discontinue its use.

The duration of PrEP use will depend on whether the person's risk of HIV continues over time. PrEP should only be prescribed to those patients who are able to adhere to a regimen that has been shown to be efficacious and who express a willingness to do so.

Adherence to PrEP should be assessed at each follow-up visit. PrEP users who explain that they have had suboptimal adherence, but who are willing and suitable to continue on PrEP, should be offered additional adherence education (see **Medication adherence**, including offering referral to peer-based support services).

If a PrEP user repeatedly reports adherence that is sufficiently suboptimal to compromise both PrEP's efficacy (i.e. fewer than four tablets per week when taking a daily regimen) and the patient's safety, the clinician should discontinue prescribing PrEP. See also Chapter 10. nPEP and PrEP for the course of action to follow if a patient is not adherent to PrEP and has had a risk of exposure in the last 72 hours.

PrEP script duration including extension of PrEP scripts

The initial and ongoing prescriptions should offer a 90-day medication supply. PrEP scripts can be dispensed and filled on the same day as the baseline HIV test is done as long as the clinician is confident that the pathology service they use will provide a 4th generation HIV test result within 24-48 hours, at which time HIV antiretroviral treatment can be offered if the HIV test is found to be positive.

Typically, PrEP prescriptions should cover no more than 90 days of TD*/FTC supply at a time. Scripts can be provided and dispensed before the repeat quarterly HIV test results are available. However, people who are travelling overseas for prolonged periods may be given more than 90 days supply of PrEP, but the patient should agree to undergo HIV and STI testing at the usual 90-day period when they are overseas and to provide the results to their PrEP prescriber in Australia. People who use on-demand† PrEP should also present for HIV and STI testing on a quarterly basis even if they do not need a prescription refill at that time.

Laboratory and clinical follow-up schedule at baseline and follow-up

The recommended schedule of testing and follow-up of people on PrEP is outlined in Table 7.1 in Clinical follow-up and monitoring of patients on PrEP.

Indicated medication

The medications proven safe and effective, and currently approved by the TGA for PrEP in healthy adults at risk of acquiring HIV infection, are the fixed-dose combination of TD* and FTC in a single daily dose. Therefore, TD*/FTC or other generic versions of TD*/FTC are the recommended medications that should be prescribed for PrEP for MSM, transgender and gender-diverse people, heterosexuals and PWID who meet recommended criteria. TDF alone has been proven effective in trials with people who inject drugs and heterosexuals (with efficacy comparable to TDF/FTC) **(19)**. As a result, WHO recommends that TDF alone can be considered as an alternative regimen in these specific populations. TDF alone is not recommended as PrEP for MSM, because no trials have been performed to assess the efficacy of this regimen in MSM.

There have been some overseas reports of HIV seroconversion in MSM taking unprescribed antiretroviral medication for PrEP **(20)**.

What not to use for PrEP

DO NOT use any HIV antiretroviral medications, either in place of, or in addition to TD* or FTC.

Do not provide PrEP as expedited partner therapy (i.e. do not prescribe for a person who is not in your care).

PrEP dosing schedule

A daily PrEP regimen involves the person taking a single daily tablet at approximately the same time each day. Taking the tablet some hours earlier or later than usual will not adversely influence the levels of the drug. If the person forgets to take a tablet for one day, there is no need to take two tablets the next day.

The on-demand† PrEP regimen involves the person taking a loading dose of PrEP where two tablets of PrEP are taken together as early as 24 hours before sex, or as late as 2 hours before sex. After sex, another PrEP tablet is taken 24 hours after the loading dose and then a final PrEP tablet is taken 48 hours after the loading dose. This 2+1+1 method for the use of on-demand† PrEP for an isolated act of sex has been endorsed by WHO **(6)**.

If more sex acts take place over the following days, a single PrEP pill can be continued daily for as long as sex continues, with a single daily pill taken for each of two days after the last sex act.

PrEP medication side effects

Patients taking PrEP should be informed of TD*/FTC side-effects experienced by participants in PrEP trials. These include headache, nausea, flatulence and the potential for renal injury. Hepatotoxicity can occur but it is very uncommon. In these trials, side-effects were uncommon and usually resolved within the first month of taking PrEP (known as 'start-up syndrome'). Clinicians should discuss the use of over-the-counter medications for headache, nausea and flatulence should they occur. Patients should also be counselled about symptoms that indicate a need for urgent evaluation (e.g. those suggesting possible acute renal injury or acute HIV infection). See **Clinical assessment before starting PrEP** for a review of the signs and symptoms of acute HIV infection.

PrEP medication drug interactions

In addition to the safety data obtained in PrEP clinical trials, data on drug-drug interactions and longer-term toxicities have been obtained by studying the component drugs individually for their use in treatment of people with HIV infection. Studies have also been performed in small numbers of healthy adults without HIV infection. No significant effect was seen, and no dosage adjustment was necessary for TD*, but there are no data on FTC **(21, 22)**.

FTC and TD* are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion. Since both drugs are primarily eliminated by the kidneys, co-administration of TD*/FTC with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of TD*, FTC and other renally eliminated drugs including (but not limited to) cidofovir, aciclovir, valaciclovir, ganciclovir, valganciclovir, aminoglycosides and high-dose or multiple non-steroidal anti-inflammatory drugs **(21)**.

Cocaine, methamphetamine and alcohol use were not seen to influence the concentrations of PrEP drugs **(23)** but use of these drugs may have an effect on the person's ability to maintain full adherence to PrEP.

Time to achieving and maintaining protection

The pharmacokinetics of TD* and FTC vary by tissue **(24)**. Data from exploratory pharmacokinetic studies conducted with men and women without HIV infection suggest that maximum intracellular concentrations of tenofovir diphosphate are reached in blood after approximately 20 days of daily oral dosing **(25, 26)**. Current evidence suggests that for both rectal and vaginal exposure, high protection is achieved after 7 days of daily dosing **(27)**. Women need to maintain high adherence to daily dosing of TD*/FTC to maintain adequate drug levels in vaginal/cervical tissues **(27)**. No data are yet available about intracellular drug concentrations in penile

tissues susceptible to HIV infection to inform considerations of protection for male insertive sex partners. Limited data exist for transgender and gender-diverse people therefore extra attention to daily dosing is recommended.

Recently WHO recommended that because cis men and other AMAB people not on exogenous oestradiol-based hormones achieve highly protective levels of PrEP medications with a single loading dose of two PrEP tablets **(28, 29)**, they can take this PrEP loading dose whether they intend to commence daily, or on-demand† PrEP **(6)**. **The ASHM PrEP Guidelines Panel agrees with this recommendation on PrEP dosing initiation for these patients whether they are commencing daily or on-demand† PrEP.**

PrEP and travel

PrEP and travel PrEP can play an important role in preventing HIV infection in people travelling outside of Australia, along with other measures to reduce HIV and STIs **(30)**. If a patient wants to take daily PrEP while on an overseas trip, they can commence two tablets on the day of departure and cease PrEP once it is no longer needed (see section below on ceasing PrEP). Alternatively, suitable patients can take a double-dose 2-24 hours before sex and then use the on-demand† regimen outlined above during the overseas trip. Cisgender women and transgender people, including those who inject drugs, who want to take PrEP while on an overseas trip should commence PrEP 7 days before their departure.

nPEP use and PrEP

If a person is not taking PrEP but presents within 72 hours of a potential HIV exposure, they should be assessed for non-occupational post-exposure prophylaxis (nPEP) as a matter of urgency and should be offered nPEP immediately according to current **nPEP guidelines** if appropriate if HIV acquisition risk is likely to continue into the future, PrEP should be offered.

Discontinuing PrEP

Clinicians should regularly advise people using PrEP about how to discontinue PrEP. The need for PrEP may end when a partner with HIV achieves sustained HIV viral suppression after at least 6 months of antiretroviral therapy, when a patient enters a mutually monogamous relationship with a seroconcordant partner, or when other social circumstances change.

Discontinuing daily PrEP in cisgender men

There is now substantial clinical evidence that cisgender men can safely cease daily PrEP by taking a dose of PrEP 24 and 48 hours after their last at-risk sexual exposure **(9-11)**. Recently WHO recommended that cisgender men who take either daily or on-demand† PrEP can safely cease PrEP by taking a dose of PrEP 24 and 48 hours after the first two pills if taking event based or if taking daily PrEP, they can cease PrEP by taking a single daily pill for each of two days after the last sex act **(6)**. **The ASHM PrEP Guidelines Panel agrees with this recommendation.**

Discontinuing daily PrEP for other populations

One US study recommends that PrEP should be continued for 28 days after the last at-risk sexual exposure **(31)**. The ASHM PrEP Guidelines Panel recommends that clinicians should offer this advice for all people other than cisgender men using daily PrEP until more information is available.

Discontinuing on-demand† PrEP

On-demand† PrEP can be ceased by taking a single daily PrEP tablet for 2 days after the last sex act, as described above.

Upon discontinuation for any reason, the following should be documented in the health record:

- HIV status at the time of discontinuation
- Reasons for PrEP discontinuation
- Recent medication adherence and reported sexual risk behaviour.

Recommencing PrEP

Clinicians should advise any patient who has discontinued PrEP on how to safely recommence PrEP. Clinicians should advise that if and when a patient decides to recommence PrEP that they must first have repeat HIV testing in case they have acquired HIV infection during the time that they were not taking PrEP. All other baseline clinical and laboratory evaluations need to be repeated also when a patient recommences PrEP and quarterly visits for PrEP scripts and ongoing evaluations must follow thereafter.

Patients may want to recommence PrEP when:

- entering a period of engaging in condomless sex
- leaving a long-term relationship
- starting a new relationship with an HIV-positive partner who is not on antiretroviral treatment, or a partner whose HIV status is unknown
- travelling to or moving to a new region or country with high or unknown prevalence of HIV during which time they anticipate that they will be having condomless sex with casual partners, or using injectable drugs
- commencing, or recommencing sex work
- returning home to an overseas country which has a high HIV prevalence during which time they anticipate that they may have condomless sex, or injecting drug use with HIV-positive partners not on antiretroviral treatment or partners whose HIV status is unknown
- entering, or leaving institutional or correctional facilities with the anticipation that they may have condomless sex, or injecting use with HIV-positive partners not on antiretroviral treatment or partners whose HIV status is unknown.

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7. Providing Injectable PrEP

Introduction and the Australian Context

On the 8th of August 2022, the Australian Therapeutic Goods Administration (TGA) approved the use of long-acting injections of cabotegravir (CAB-LA) as HIV pre-exposure prophylaxis (PrEP) for adults and adolescents with HIV acquisition risk (for those at least 12 years of age and weighing at least 35 kg). In September 2023, the Pharmaceutical Benefits Advisory Committee (PBAC) recommended that CAB-LA be listed on the general schedule (with streamlined authority) for use as PrEP. The National PrEP Guidelines committee originally published this guidance on the 1st of December 2023. As of the 12th of June 2024, CAB-LA has not been subsidised on the Pharmaceutical Benefits Scheme as a pricing agreement between ViiV Healthcare and the Pharmaceutical Benefits Advisory Committee could not be reached.

This ASHM guideline is intended to provide clinicians with relevant information and evidence on CAB-LA PrEP, recognising the potential for this HIV prevention technology to become available in Australia in the future. It also acknowledges that clinicians may require this information if they encounter patients who have received CAB-LA PrEP overseas.

Evidence for effectiveness

The HIV Prevention Trials Network (HPTN) assessed the effectiveness of CAB-LA for the prevention of HIV infection in two multisite randomised controlled trials (RCTs), namely HPTN-083 and HPTN-084 **(1, 2)**. With a similar design, these trials assessed effectiveness in different populations: HPTN-083 enrolled 4,566 cisgender men who have sex with men (MSM), and transgender women (12.5% of participants) who have sex with men, across 43 trial sites in the United States, Latin America, Africa, and Asia; whereas HPTN-084 enrolled 3,224 cisgender women across seven countries in sub-Saharan Africa.

In both trials, CAB-LA PrEP injections commenced after an oral lead-in phase, and participants were randomised (1:1) to receive either 8-weekly CAB-LA injections and daily oral placebo pills, or 8-weekly placebo injections and daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC). TDF/FTC is no longer available in Australia, having been replaced with several therapeutically equivalent generic versions of tenofovir, hereafter referred to as TD*/FTC.

Participants were followed for 153 weeks, with the primary endpoint being incident HIV infections. Among MSM and transgender women, HPTN-083 estimated a 66% reduction in HIV risk (hazard ratio 0.34; 95% confidence interval (CI) 0.18 to 0.62) with CAB-LA compared with oral TDF/FTC. This superiority finding of CAB-LA versus oral TDF/FTC may not be translatable to the Australian context, due to very low HIV diagnosis rates among Australian PrEP users **(3, 4)**. In HPTN-083 and its subsequent open label extension, 34 HIV infections occurred in the CAB-LA group, of which six occurred in participants with appropriately timed CAB-LA doses and adequate plasma cabotegravir concentrations **(5)**.

Among cisgender women, HPTN-084 estimated an 88% reduction in HIV risk (hazard ratio 0.12; 95% CI 0.05 to 0.31) with CAB-LA compared with oral TDF/FTC. Four HIV infections occurred in the CAB-LA group, of which one infection occurred during the CAB-LA injection phase (rather than during the oral lead-in phase), and that participant had delayed injection visits and suboptimal plasma cabotegravir levels.

Pharmacokinetic studies have shown that three days after a single IM injection of CAB-LA 600mg, all participants had plasma cabotegravir concentrations that were four times the in vitro protein-adjusted 90% maximal inhibitory concentration (PA-IC_{90}), and concentrations in rectal fluid peaked by day eight, indicating a rapid onset of action of CAB-LA **(6)**.

Safety and Adverse Effects

Cessation due to adverse effects

Permanent discontinuation of PrEP due to adverse effects was uncommon in both HPTN-083 and HPTN084, at 3.8% and 1.2% of participants respectively. In both trials, the discontinuation rate due to adverse effects was similar in the active CAB-LA and TDF/FTC arms.

Safety and systemic adverse effects

Adverse events rated grade 2 or higher were common in both HPTN-083 and HPTN-084, occurring in 92.5% and 92.2% of participants respectively, and similar between the active CAB-LA and TDF/FTC arms, apart from injection site reactions (ISRs) being more common in the active CAB-LA arms (discussed below). Adverse events rated grade 3 or higher included increased serum creatinine, increased lipase, and increased liver enzymes, all affecting <5% of participants across trials and were similar between the CAB-LA and TDF/ FTC arms.

Injection-site reactions

ISRs were common in both HPTN trials. In HPTN-083, 81.4% of participants in the active CAB-LA arm complained of ISRs, compared with 31.3% in the TDF/FTC (placebo injection) arm. In HPTN-083, permanent discontinuation was strongly associated with higher-severity ISR from CAB-LA injections, and in total 2.4% of participants in the CAB-LA arm discontinued due to ISRs. In HPTN-084, 38.0% of participants in the CABLA arm complained of ISRs, compared with 10.8% in the TDF/FTC (placebo injection) arm, but no participants discontinued due to ISRs.

ISRs were usually rated as mild-to-moderate and typically lasted only a few days. Patients should be warned about these ISRs, but also reassured that ISRs usually improve after the initial 2-3 injections. The following advice can help to reduce the severity of ISRs:

- Pro-actively take simple analgesia or NSAIDS a couple of hours prior to the scheduled CAB-LA injection and continue taking these if required for one or two days after.
- Apply a warm compress to the injection site for 15-20 minutes after the injection.

Weight gain

In HPTN-083, participants in the CAB-LA arm gained 1.23 kg per year (95% CI 1.05 to 1.42) and those in the TDF/FTC arm gained 0.37 kg per year (95% CI 0.18 to 0.55). Similarly, in HPTN-084, participants in the CAB-LA group gained slightly more weight than those in the TDF/FTC group.

HIV acquisition during CAB-LA use: Drug resistance mutations and delayed diagnosis.

In HPTN-084, no major integrase strand transfer inhibitor (INSTI) resistance mutations were detected in any of the four HIV infections observed in the CAB-LA group.

In HPTN-083 and its open label extension, INSTI resistance mutations were detected in ten of the 18 cases who had at least one CAB-LA injection in the six-month period prior to their first positive HIV test **(5)**. Participants who acquired HIV had delayed diagnoses due to suppression of viral load and attenuation of the HIV antibody response, and this delayed detection contributed to the development of INSTI resistance mutations **(5, 7, 8)**. If HIV RNA tests had been used for screening, rather than standard 4th generation HIV Ag-Ab serology, the majority of infections would have been detected earlier. Retrospective analysis of HPTN-083 and its open label extension suggests that HIV RNA screening would have detected these infections before participants developed INSTI resistance in 75% (6 of 8) cases **(8)**. In response, the United States PrEP

guidelines now recommend the use of HIV RNA tests to screen for HIV infection in people who are using PrEP (oral or injectable) **(9)**. However, The impact of this HIV RNA screening strategy on time to diagnosis and prevention of INSTI resistance has not been prospectively studied. In Australia, the use of HIV RNA tests is strictly regulated and no HIV RNA tests have been approved for HIV screening in the setting of HIV PrEP use. HIV RNA alone is not a diagnostic test for HIV in adults and a negative test does not rule out HIV. In addition, HIV RNA tests are not Medicare-rebated for HIV screening. The World Health Organization recommends that in-country guidelines should use the national HIV testing algorithm for HIV screening in people using CAB-LA PrEP **(10)**, and we have adopted this approach in these guidelines.

Suitability for CAB-LA PrEP

Note: As of 12 June 2024, CAB-LA PrEP is NOT listed on the PBS and is unavailable for use in Australia.

When the TGA approved the use of CAB-LA in at-risk adults and adolescents (at least 12 years of age and weighing at least 35 kg) for the prevention of sexually transmitted HIV infection, it stipulated that patients must have a documented negative HIV test prior to initiation of CAB-LA for PrEP. Patients have the option of a one-month oral cabotegravir lead-in phase prior to the first CAB-LA injection, or patients may opt to initiate directly onto CAB-LA injections without an oral lead-in.

The ASHM PrEP guidelines committee advocates for informed patient decision making when selecting a PrEP regimen, including daily oral PrEP (TD*/FTC or TAF/FTC), on-demand oral PrEP, and when available - CAB-LA injectable PrEP.

The suitability criteria listed below are designed to assist practitioners to determine the suitability of CAB-LA PrEP for individual patients. Note that the effectiveness of CAB-LA PrEP has been studied only among GBMSM and cisgender women, not among cisgender heterosexual men, nor among people whose main HIV risk is intravenous drug use. However, there is no known reason why CAB-LA PrEP should not be effective in these populations, and hence these guidelines recommend that CAB-LA PrEP should be considered as an option for anyone who is at risk of HIV.

The following harm reduction strategies should additionally be offered to people who inject drugs:

- Access to clean injecting equipment through “needle-and-syringe programmes”.
- Access to take-home naloxone, which is available through pharmacies. This is relevant to anyone who uses opioids or anyone who is likely to witness opioid use, but also for people who inject other drugs that can be contaminated with opioids.

These first two suitability criteria are crucial for any patient considering CAB-LA PrEP:

1. **The patient is at risk of HIV if PrEP is not prescribed:** See main PrEP guidelines for HIV risk guidance.
2. **The patient is currently HIV-negative:** A recent negative HIV test result must be available prior to the first CAB-LA injection, ideally within the prior 7 days, or up to 4 weeks prior in a patient with no recent HIV risk (e.g. if they are adherent to oral PrEP, or not sexually active, in the past six weeks).

The following factors are relevant when assessing a patient’s suitability for CAB-LA PrEP:

The patient has medical contraindications to oral TD*/FTC, such as renal impairment and/or low bone mineral density. Of note, most patients with these conditions will be able to safely use oral tenofovir alafenamide with emtricitabine (TAF/FTC), which is also approved by the TGA for daily oral PrEP, but not PBS-listed. TAF/FTC is expensive when purchased privately in Australian pharmacies, but can be imported affordably, under the TGA’s personal importation scheme (see main **PrEP guideline section on TAF/FTC**).

1. For a PrEP-experienced patient, the clinician has documented prior and/or current difficulties adhering to oral PrEP.
2. For a PrEP-naïve patient, the clinician anticipates that the patient will have difficulties adhering to oral PrEP due to medical, mental health and/or psychosocial factors.
3. The patient reports potential barriers to adherence to oral PrEP. This may include difficulty remembering to take tablets, and concerns around privacy when needing to store PrEP tablets. The latter may be particularly relevant for people who live in shared accommodation, and who have not disclosed their sexual practices to their co-habitants, those who are experiencing homelessness, or those who may be at risk of intimate partner violence.
4. The patient is willing to have an intramuscular injection every two months, recognising that these can be painful and associated with injection site reactions.
5. The patient's life circumstances can incorporate ongoing CAB-LA injection visits every two months. For example, it may be difficult to attend these visits for patients who travel frequently, or have limited financial resources or complex social/family dynamics. Importantly, planned missed visits can be bridged with oral cabotegravir tablets, but unplanned missed visits may result in HIV risk with the additional risk of cabotegravir resistance (see section on missed injection visits).
6. The patient understands the concept of the long pharmacokinetic tail of CAB-LA, and once CAB-LA is ceased they will need to use some form of effective HIV prevention for at least twelve months after their final CAB-LA injection.

Contraindications to CAB-LA PrEP

Absolute contraindications to CAB-LA PrEP

- HIV infection or unknown HIV status
- Insurmountable barriers that will likely prevent regular attendances for CAB-LA injection appointments
- Known hypersensitivity to cabotegravir or excipients in the tablets or injection formulation
- **Drug-drug interactions.** Cabotegravir is primarily metabolised by uridine diphosphate glucuronosyl transferase (UGT) 1A1, with some contribution from UGT1A9. Medications that are strong inducers of these enzymes will reduce efficacy of CAB-LA PrEP. For this reason, CAB-LA PrEP is contraindicated in people receiving rifampicin, rifapentine, phenytoin, phenobarbital, carbamazepine, or oxcarbazepine. CAB-LA PrEP users need to be informed of the risk of drug-drug interactions, and the need to inform other prescribers of their CAB-LA PrEP use prior to the initiation of any new medication. Further guidance is available from the HIV drug interaction checker from the University of Liverpool: **https://www.hiv-druginteractions.org/checker**

Other safety considerations

1. **Renal impairment:** Cabotegravir has a favourable renal safety profile, and no dosage adjustment is required for individuals with renal impairment who are not on dialysis **(11)**. Serum creatinine rises were observed in a small number of individuals receiving CAB-LA in HPTN-083 and HPTN-084, and hence these guidelines currently recommend monitoring of renal function (by serum creatinine and eGFR) during CAB-LA use, until more renal safety data are accumulated. In the event of a significant deterioration in renal function, prescribers are advised to seek advice from an experienced CAB-LA prescriber or a renal physician experienced with antiretrovirals.
2. **Hepatic impairment and toxicity:** No dosage adjustment is required for individuals with mild to moderate hepatic impairment (Child-Pugh A or B). CAB-LA has not been studied in individuals with severe hepatic

impairment (Child-Pugh C). These guidelines currently recommend monitoring of liver transaminase levels during CAB-LA use, until more liver safety data are accumulated. In the event of a significant deterioration in liver function, prescribers are advised to seek advice from an experienced CAB-LA prescriber or a hepatologist experienced with antiretrovirals.

3. **Hepatitis B virus (HBV) infection:** Unlike some other HIV antivirals, CAB-LA has no activity against HBV. Hence, people who need both HBV treatment and HIV PrEP, should be recommended a HIV PrEP regimen that also treats HBV, such as daily oral TD*/FTC or daily TAF/FTC. Also, if people with HBV are switched to CAB-LA from daily oral TD*/FTC or TAF/FTC, this switch could result in a flare of their HBV infection. It is also important to consider that for people who have no immunity to HBV (i.e. who are HBsAb negative), CAB-LA will not offer protection against HBV infection, unlike TD*/FTC or TAF/FTC **(12)**. See the **PrEP Guidelines section on HBV** for further information.
4. **Hepatitis C virus (HCV) infection:** CAB-LA has no activity against HCV. Every person diagnosed with HCV should be recommended to access HCV treatment using direct-acting antivirals (DAAs).
5. **Adolescents and children:** The safety and efficacy of CAB-LA has not been established in children < 12 years of age or in people weighing less than 35kg.
6. **Elderly:** No dosage adjustment is required in elderly individuals, but data are limited in individuals aged 65 years and over.
7. **Pregnancy:** Category B1 Data on cabotegravir in pregnancy are limited, and the effect of CAB-LA on human pregnancy is unknown. Women and other people capable of childbearing should be provided with contraceptive advice prior to commencement of CAB-LA, and CAB-LA should only be used during pregnancy if the expected benefit justifies potential risks to the foetus. It should be noted that cabotegravir has been detected in systemic circulation for up to 12 months or longer after a CAB-LA injection.
8. **Hypersensitivity reactions:** Rarely, use of other INSTIs has been associated with hypersensitivity reactions, which are characterised by skin rash and sometimes organ dysfunction, including liver injury. To date, no such reactions have been observed with CAB-LA.
9. **Patients with a history of buttock augmentation surgery** will need to be assessed for the presence and location of implants to see if it is safe to commence CAB-LA. Injection of CAB-LA into an implant will render CAB-LA ineffective.
10. **HIV resistance mutations:** If an individual initiates CAB-LA in the context of undiagnosed HIV, or if they acquire HIV during use of CAB-LA, then their HIV virus can develop resistance to cabotegravir, which may also confer resistance to other INSTI-based HIV treatments. See section titled "**Managing HIV diagnoses during CAB-LA PrEP**".

Practicalities of delivering CAB-LA PrEP injections

Prior to administration of CAB-LA PrEP, clinicians should familiarise themselves with the administration instructions contained in the packaging.

Storage and transport of cabotegravir injections

CAB-LA vials can be stored at room temperature, and do not need to be refrigerated.

Self-administration

Self-administration of CAB-LA injections is currently not recommended.

Starting CAB-LA PrEP

ASHM recommends a two-appointment approach (outlined in box 7.1) when initiating CAB-LA PrEP, but under certain circumstances it may be safe to initiate CAB-LA PrEP in a single appointment, as outlined below.

BOX 7.1 THE TWO-APPOINTMENT APPROACH

Commencement appointment 1:

1. Ascertain whether the patient would benefit from taking PrEP. See full ASHM PrEP guidelines for HIV risk guidance: https://prepguidelines.com.au/
2. Assess suitability for CAB-LA PrEP, as described in the section "Suitability for CAB-LA PrEP".
3. If a patient wishes to commence CAB-LA PrEP, discuss the need to commit to having ongoing two-monthly injection visits and discuss how they might achieve this. For example, by setting recurring two-monthly phone reminders to make clinic appointments. Subsequent injections can be administered up to seven days before or after the scheduled injection date, and hence for some people it may be useful to set recurring reminders to occur seven days before the scheduled injection date, to provide a 14-day administration window.
4. Assess for signs and symptoms of acute HIV infection (see https://prepguidelines.com.au/).
5. Perform laboratory testing:
   a. Laboratory-based HIV serology. In the context of CAB-LA PrEP use, clinicians must not rely solely on point-of-care HIV rapid tests to determine HIV status, however, HIV point- of-care tests can be used as an adjunct to HIV serology for same-day initiation of CAB-LA (see below).
   b. Renal function testing by serum creatinine and eGFR.
   c. Liver function tests
   d. Screening for sexually transmissible infections and viral hepatitis, as specified in the Australian STI Management Guidelines – https://sti.guidelines.org.au
6. Consider as an option, the immediate commencement with the oral lead-in phase using cabotegravir tablets. The purpose of the oral lead-in phase is to exclude significant adverse effects prior to giving the first long-acting cabotegravir injection. However, because no significant safety concerns were identified during the phase III trials, this oral lead-in phase is optional. As further discussed under the heading "Same day initiation", there are currently insufficient data to indicate that the oral cabotegravir lead-in phase will rapidly control a patient's HIV risk, and those patients who require rapid HIV protection could immediately start oral TD*/FTC or TAF/FTC while preparing to commence CAB-LA injections.
7. Provide the patient with a prescription for CAB-LA, in preparation for appointment 2.

Commencement appointment 2:

1. Once the HIV test result is available, initiate injectable CAB-LA, ideally within one week after the HIV test is performed.
2. Address any other abnormalities found on laboratory testing, e.g., sexually transmitted infections. If renal and/or liver function test results are abnormal, this need not delay initiation of CAB-LA injections, but should prompt appropriate investigation and follow-up. In the case of severe derangements of renal and/or liver function, the clinician may choose to defer commencing CAB-LA pending further investigations and then will need to explore alternative HIV prevention strategies with the patient in the interim.
3. Administer cabotegravir 600mg IM into the ventrogluteal muscle using a needle that is long enough to deliver this into the intramuscular space. For patients with a body mass index (BMI) of less than 30 this can be achieved with a 1.5-inch (38mm) needle, but for patients with an BMI of 30 or greater this requires a 2.0-inch (50mm) needle.
4. Educate the patient on how to manage injection site reactions (ISRs) (see section "Safety and Adverse Events").
5. Remind the patient that they may not immediately be protected against HIV. The time to optimal protection is unclear, but should be no more than a few days to one week (6, 13). People who require immediate HIV protection may initiate or continue TD*/FTC or TAF/FTC simultaneously as CAB-LA, and continue TD*/FTC or TAF/FTC for one week after commencement of CAB-LA.
6. Arrange the next visit one month after the first injection, to receive their second injection.

First follow-up – One month after first CAB-LA injection

1. Review the patient's satisfaction with CAB-LA, and review their understanding of the need for ongoing 2-monthly visits after this visit. If the patient does not wish to continue with CAB-LA, then discuss switching to oral PrEP using TD*/FTC or TAF/FTC.
2. Assess for signs and symptoms of acute HIV infection.
3. Order repeat laboratory-based HIV serology, eGFR and LFTs.
4. Arrange an appointment in 2 months' time for their next CAB-LA injection.

Same-day initiation

In some instances, it may be safe to initiate CAB-LA PrEP at a patient's first visit. For example, a patient who has had no significant HIV risk or has been adherent to oral PrEP over the preceding six weeks, and whose HIV rapid point of care test is non-reactive on the day of initiation (while awaiting a laboratory HIV serology result).

If a same-day initiation approach is taken, then the patient needs to understand that they must return to the clinic immediately if their laboratory HIV serology returns a positive result, to consider immediate initiation of HIV treatment to avoid generating INSTI resistance mutations.

The patient needs to be informed that same-day initiation may not mean same-day protection, as the time to optimal protection is not known, and may be a few days to one week after initiation **(6, 13)**. People who need immediately effective HIV prevention can be offered immediate commencement of oral TD*/FTC or TAF/FTC at the same time as CAB-LA, and to continue oral PrEP for one week after starting CAB-LA.

Transferring from oral PrEP (TD/FTC or TAF/FTC) to CAB-LA PrEP*

ASHM recommends a similar approach to transferring from oral PrEP to CAB-LA PrEP as the approach outlined above, with some minor differences:

1. Patients can continue to use oral TD*/FTC or TAF/FTC for PrEP until the day of their initial CAB-LA injection, instead of using an oral cabotegravir lead-in.
2. Recent/current oral PrEP use can interfere with the accuracy of HIV tests, both standard serology and rapid tests, in terms of their sensitivity. Hence at the time of transfer to CAB-LA PrEP, clinicians should be careful to ask about PrEP adherence over the preceding six weeks.
3. Patients with immediate HIV risk can consider continuing on oral PrEP for one week following commencement of CAB-LA.

Ongoing Monitoring During CAB-LA PrEP

The aims of laboratory and clinical monitoring during CAB-LA PrEP are similar to those of monitoring during oral PrEP, and consist of testing for HIV and STIs, and monitoring for adverse effects. The main difference between monitoring protocols for CAB-LA PrEP vs oral PrEP is that CAB-LA visits must occur every two months, whereas oral PrEP visits are recommended to occur every three months.

At each bimonthly CAB-LA monitoring visit:

1. Review satisfaction with CAB-LA PrEP, and ongoing need;
2. Perform laboratory-based HIV serology;
3. Perform renal function (serum creatinine) and liver function testing;
4. Administer CAB-LA injection.

In addition, patients should be offered STI and BBV screening at an interval relevant to their STI/BBV risk profile. For example:

- For gay, bisexual and other men who have sex with men (GBMSM), including transgender men who have sex with men, and transgender women who have sex with men:
  - Offer STI testing either every visit (i.e. every two months) or every second visit (i.e. every four months), depending on the patient's preference and STI risk profile. For these populations, in the context of increasing syphilis incidence and its associated morbidity, syphilis serology should be offered at every visit, with screening for chlamydia and gonorrhoea on swabs and urine less frequently.
- For heterosexually active cisgender women and cisgender men:
  - STI screening is recommended at 6-monthly intervals, and consists of syphilis serology and screening for chlamydia and gonorrhoea, which may not need to be performed at all three anatomical sites. In populations with high rates of syphilis, it is recommended to perform syphilis serology every two months.
- Hepatitis C antibody testing is generally recommended annually. For people who inject drugs, hepatitis C testing is recommended every six months. Anyone who has previously had a hepatitis C infection should be tested by HCV RNA rather than HCV Ab.

Managing Missed CAB-LA Injection Visits

If a patient misses a CAB-LA injection, and if they subsequently acquire HIV, then the low levels of serum cabotegravir may result in the selection of INSTI resistance mutations, which then limit HIV treatment options. As such, it is very important to proactively consider the possibility of missed injection visits, and plan to avoid their occurrence.

CAB-LA injections can be given up to 7 days before, or after the scheduled dosing date without being classed as "missed" injections, and for some patients it may be useful to plan to administer the injections one week early, so that the patient then has a two-week window to reschedule any missed appointments.

If the missed CAB-LA injection is the second injection (i.e. one month after the initiation injection), then:

- If the CAB-LA injection is administered within 2 months of the initiation injection, then administer the injection and continue with 2-monthly dosing.
- If the CAB-LA injection is administered more than 2 months after the initiation injection, then re-start the initial dosing schedule. As in, the next injection will be planned for one month after the recommencement injection, then followed by resumption of the 2-monthly dosing schedule.

If the missed CAB-LA injection is the third or subsequent injection, then:

- If the CAB-LA injection is administered within 3 months of the last injection, then administer the injection and continue with 2-monthly dosing.
- If the CAB-LA injection is administered more than 3 months after the last injection, then re-start the individual on one CAB-LA injection, followed by a second CAB-LA injection one month later, then resume the 2-monthly dosing schedule.

If a patient misses their CAB-LA injection appointment by more than 7 days after the 2-month mark, and if this break is not covered by oral PrEP (either cabotegravir, TD*/FTC or TAF/FTC), then they should have a repeat HIV test before re-starting CAB-LA injections, and another HIV test one month after re-starting CABLA injections.

If a patient plans to miss their next injection appointment, for example because they are planning a long overseas holiday, then they can be supplied with cabotegravir tablets (30mg) to be taken once daily, starting two months after their last injection visit (i.e. when due for their next CAB-LA injection), for a duration of up to two months, and up until their next injection visit. If the planned break from injections is greater than two months (i.e. more than four months between injection visits), then an alternative oral PrEP regimen is recommended, such as oral TD*/FTC or TAF/FTC, to be continued until the day of their next CAB-LA injection visit.

Following an interruption to 2-monthly CAB-LA dosing, if the time since their last CAB-LA injection is longer than 3 months, then they should follow the re-initiation protocol: re-start the individual on one CAB-LA injection, followed by a second CAB-LA injection one month later, then resume the 2-monthly dosing schedule. This applies even if their interruption was covered by either cabotegravir tablets or oral TD*/FTC or TAF/FTC.

Planning for Cessation of CAB-LA PrEP

Patients who wish to cease CAB-LA PrEP should be reminded of the long pharmacokinetic tail of CAB-LA, and hence the risk of developing INSTI resistance mutations if they acquire HIV during the twelve months after their last injection. Patients should be advised to use oral PrEP during the twelve months following their last CAB-LA injection if they have ongoing risk of HIV acquisition.

The following strategy is recommended for people with ongoing HIV risk to mitigate the risk of developing drug-resistant HIV after stopping CAB-LA PrEP:

1. Two months after their last CAB-LA injection, commence an alternative form of PrEP. For example, people at risk who are frequently sexually active could use daily oral TD*/FTC or TAF/FTC; while people at risk who are infrequently sexually active could use on-demand TD*/FTC for sexual activities that may place them at risk of HIV (but only if they meet the suitability criteria for on-demand PrEP, as outlined in the PrEP guidelines).
2. In the rare instance when a patient cannot tolerate either daily or on-demand TD*/FTC or daily TAF/FTC, consistent use of condoms is the preferred HIV prevention method.
3. Attend every three months for HIV serology, for at least 12 months after their last CAB-LA injection.

Managing an ambiguous HIV result during CAB-LA PrEP

An ambiguous or inconclusive HIV result may occur when a 4th generation Ag-Ab screening test is reactive and confirmatory testing, such as a Western Blot, is indeterminate. This may be due to recent infection or may represent a false-reactive result. Urgent HIV nucleic acid amplification testing is required to determine the individual's HIV status, especially in the setting of CAB-LA PrEP use.

1. Ask the patient to return to the clinic as soon as possible.
2. If the CAB-LA prescriber is not an experienced HIV prescriber, then they should seek immediate advice from a local tertiary HIV service or an expert HIV clinician.
3. The prescriber is advised to speak to the testing laboratory to confirm which follow-up tests should be requested when the patient returns to the clinic. This will likely include a dedicated whole blood sample for HIV proviral DNA and/or qualitative HIV RNA testing. Also consider collecting a whole blood sample for a HIV genotype resistance assay (GRA) including INSTI mutations, in case the HIV result is confirmed to be a true positive.

4. When the patient returns to the clinic:
    a. Explain the inconclusive HIV result and need for further testing.
    b. Perform further testing as advised by the laboratory.
    c. Discuss the possibility of immediate commencement of protease inhibitor-based treatment (e.g. Symtuza®), while awaiting confirmatory results. This will require discussion with a tertiary HIV service, as 3-drug antiviral regimens are only available on the PBS for people with confirmed HIV, and a private prescription is likely to be cost-prohibitive.
    d. Offer the patient linkage to a counsellor or peer-support organisation.
    e. Arrange clinical review once further HIV testing results are available.
5. Liaise with the laboratory to advise that specimens are being sent for urgent testing and request urgent notification of results as soon as they are available.
6. If 4th generation Ag-Ab testing is reactive and HIV is confirmed by detection of HIV via nucleic acid amplification testing (proviral DNA and/or qualitative RNA), the patient should be managed as a new diagnosis of HIV as discussed in the section below.
7. If HIV is not detected via nucleic acid amplification testing (proviral DNA and/or qualitative RNA), a plan for close laboratory follow-up and the ongoing PrEP regimen should be made with a multidisciplinary team, including the local tertiary HIV service or expert community-based HIV clinician and the testing laboratory.

Managing an HIV Diagnosis during CAB-LA PrEP

In Australia an HIV diagnosis is made when a person has a positive HIV Ag/Ab test result which is confirmed by either a Western blot, or HIV nucleic acid testing (RNA or DNA), or with p24 Ag testing.

Please see the section above for the management of those patients who have an ambiguous HIV test result.

Managing a new HIV diagnosis during CAB-LA PrEP use may present a challenge for the clinician because evolution of HIV test results may be delayed by the presence of cabotegravir, and the patient may have developed resistance to the INSTI drug class. ASHM recommends the following approach to managing HIV diagnoses during CAB-LA PrEP use, or in the twelve months following a CAB-LA injection in someone who has ceased CAB-LA PrEP.

1. Ask the patient to return to the clinic as soon as possible.
2. If the CAB-LA prescriber is not an experienced HIV prescriber, then they should seek immediate advice from a local tertiary HIV service or an expert HIV clinician.
3. When the patient returns to the clinic:
    a. Explain the HIV result.
    b. Arrange for further testing, including a repeat HIV serology, plasma HIV RNA testing, CD4 lymphocyte count and HIV genotype resistance assay including INSTI mutations. Liaise with the receiving laboratory to ensure that the correct types and quantities of pathology tubes are collected.
    c. Either immediately commence 3-drug therapy using a PI-based regimen (e.g., Symtuza®), or arrange for urgent review by an expert HIV clinician. Do not wait for the additional test results to become available before initiating treatment.
    d. Offer the patient linkage to a counsellor or peer-support organisation.
    e. Arrange clinical review one week later to review progress.

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8.

Clinical follow-up and monitoring of patients on PrEP

Recommended schedule of testing and follow-up for people on PrEP

Once pre-exposure prophylaxis (PrEP) is initiated, patients should return for follow-up every 3 months. Clinicians may wish to see patients more frequently in the period after PrEP initiation (e.g. 1 month after initiation) to:

- assess and re-confirm human immunodeficiency virus (HIV)-negative test status in patients with a recent pre-PrEP HIV exposure
- assess side effects
- monitor renal function in patients at particular renal risk
- assess adherence
- answer questions.

Some jurisdictions recommend a visit at month one. Table 8.1 and Box 8.1 set out the recommended schedule of testing and follow-up for people who are prescribed PrEP.

Table 8.1 Laboratory evaluation and clinical follow-up of individuals who are prescribed PrEP

TEST	BASELINE (WEEK 0)	ABOUT DAY 30 AFTER INITIATING PREP (OPTIONAL BUT RECOMMENDED IN SOME JURISDICTIONS)	90 DAYS AFTER INITIATING PREP	EVERY SUBSEQUENT 90 DAYS ON PREP	OTHER FREQUENCY
HIV testing and assessment for signs or symptoms of acute infection	Y	Y	Y	Y	N
Assess side effects	N	Y	Y	Y	N
Hepatitis B serology Vaccinate if non-immune	Y	N	N	N	Y If patient required hepatitis B vaccine at baseline, confirm immune response to vaccination 1 month after last vaccine dose
Hepatitis C serology	Y	N	N	N	12 monthly but, more frequently if ongoing risk e.g. non-sterile injection drug use and MSM with sexual practices that pre-dispose to anal trauma
STI (i.e. syphilis, gonorrhoea, chlamydia) as per Australian STI Management Guidelines *	Y	N	Y	Y	N
eGFR at 3 months and then every 6 months	Y	N	Y	N	At least every 6 months or according to risk of CKD
Urine protein creatinine ratio (PCR) baseline	Y	N	Y	N	Every 6 months
Pregnancy test (for women of child-bearing age , not on effective contraception)	Y	Y	Y	Y	N

CKD: chronic kidney disease
eGFR: estimated glomerular filtration rate
PrEP: pre-exposure prophylaxis
PWID: people who inject drugs
STI: sexually transmissible infection
* http://www.sti.guidelines.org.au

BOX 8.1 PREP FOLLOW-UP PROCEDURES

At least every 3 months:

- Repeat HIV testing and assess for signs or symptoms of acute infection to document that patients are still HIV negative. Rapid point-of-care tests (POCTs) are not recommended for monitoring patients receiving PrEP
- Test for sexually transmissible infections (STIs). This involves PCR tests for chlamydia (first-pass urine, pharyngeal swab and anal swab) and Neisseria gonorrhoea, (pharyngeal swab and anal swab) and a blood test for syphilis serology (1)
- Assess side-effects, PrEP adherence and ongoing PrEP suitability
- Provide an authority streamlined (PBS) prescription or a private prescription of daily TD*/FTC for 90 days (see Providing PrEP for exceptions to this script duration)
- Respond to questions and provide any new information about PrEP use
- Provide support for medication adherence and risk-reduction behaviours.

In addition:

- Repeat pregnancy testing for women of child bearing age
- Test for hepatitis C virus (HCV) in people who inject drugs (PWID) who report continued sharing of injecting equipment and men who have sex with men (MSM) with elevated risk of HCV acquisition (e.g. sexual practices that pre-dispose to anal trauma).

At least every 6 months:

- Monitor estimated glomerular. filtration rate (eGFR), creatinine and urine protein/creatinine ratio
- If the patient has risk factors for renal impairment (e.g. hypertension, diabetes), renal function may require more frequent monitoring and/or may need to include additional tests (e.g. urine protein/creatinine ratio)
- A rise in serum creatinine is not always a reason to withhold treatment if the eGFR remains at or above 60 mL/min/1.73 m2 but an acute rise in the serum creatinine in a patient on PrEP would need full clinical evaluation and sometimes a review by a renal specialist
- If eGFR is declining steadily (but still at or above 60 mL/min/1.73 m2), consultation with a renal specialist or other evaluations of possible causes for declining renal function may be indicated.

At least every 12 months:

- Test for hepatitis C
- Test for hepatitis B serology if the patient has not been vaccinated.

Patients who access PrEP through the Personal Importation Scheme of the Therapeutic Goods Administration (TGA) should allow a lead time of 2–6 weeks for the drug to arrive in Australia and pass customs clearance.

Testing for HIV

HIV testing should be repeated every 3 months using a fourth generation HIV antibody and antigen test via a venous blood draw. Rapid point-of-care tests, including the recently approved home testing HIV diagnostic kit, the Atomo HIV Self Test, should not be used for monitoring patients receiving PrEP.

A patient's ongoing HIV risk and adherence to PrEP should be established when requesting the patient presents for their quarterly clinical visit including the HIV test and PrEP script (see Improving medication adherence). Patients should be familiar from their baseline visit with the requirement for quarterly clinical visits to obtain ongoing PrEP prescriptions. Clinicians should consider writing on ongoing PrEP prescriptions a date past which

dispensing the script should not occur without the pharmacist talking to both the patient and the prescribing doctor about the reasons for the delay in filling the script. This approach may help ensure that patients who have had intermittent PrEP adherence and who have unknowingly acquired HIV infection do not receive 3 months of suboptimal antiretroviral treatment. See Appendix 2 for up-to-date HIV tests approved in Australia (K Wilson, National Serum Reference Library, personal communication) and time to detection of HIV infection **(2)**.

A positive HIV test result

Any positive HIV test result should be managed urgently by appropriate counselling and referral to an HIV prescriber. Assistance can be sought via telephone from a local sexual health clinic. It is very important for the clinician to recognise that HIV acquisition in a person who is using PrEP is a highly significant event and that the emphasis should be on supporting the person initially rather than focusing on how the infection occurred. If a patient is diagnosed with HIV infection while taking PrEP, their current health and wellbeing should be the chief immediate priority as opposed to enquiries about their adherence to PrEP.

Acute HIV infection should be suspected in people at risk for HIV who were not taking PrEP at the time that they were recently exposed to HIV (e.g. no condom, or a condom broke during sex with an HIV-positive partner who was not on antiretroviral treatment, or has a detectable HIV viral load; condomless anal sex with a casual partner; recent injecting drug use with shared injection equipment with an HIV-positive partner). Also, infection with tenofovir disoproxil* (TD*)- and/or emtricitabine (FTC)-resistant HIV is possible, however, it is very uncommon while on PrEP, with only a few cases reported internationally **(3)**. Therefore, in addition to sexual behaviour and injecting drug use, clinicians should elicit a history of any signs and symptoms of viral infection during the preceding month, including the day of PrEP evaluation. See the Table for clinical symptoms and abnormalities of acute (primary) HIV infection.

In this setting HIV drug resistance testing should be performed in all cases and if the patient reports high PrEP adherence they may agree to have their blood, and hair tested for tenofovir and emtricitabine drug levels. In this setting urgent referral to an HIV specialist is recommended. If urgent review by an HIV specialist is not possible, then the diagnosing clinician may wish to phone ASHM who will be able to help coordinate the patient and a clinical advisor.

Indeterminate HIV test results in the first 3 months on PrEP

There is a potential for PrEP to delay or attenuate seroconversion in people who may have been exposed to HIV just before starting PrEP, or who acquire HIV infection while taking PrEP (e.g. due to poor adherence or transmitted drug resistant virus) **(4-6)**. There is not a broad international agreement on how to manage these patients. Patients who have an indeterminate HIV test result while on PrEP (particularly, those with repeated indeterminate test results) should be closely monitored in conjunction with an HIV specialist and in consultation with a diagnostic laboratory scientist who should be informed that the patient is taking PrEP. The ASHM PrEP Guidelines Panel will continue to monitor this issue with a view to providing further guidance.

A recent high-risk exposure (within 72 hours)

A course of non-occupational post exposure prophylaxis (nPEP) may be required if a patient is on daily PrEP, or on-demand† PrEP and had a recent high-risk exposure (within 72 hours) but only if they did not take PrEP during those days. This nPEP may need to consist of a three-drug regimen, depending on the nature of the exposure. See section on **nPEP and PrEP** for management of such cases.

Monitoring of renal function

Renal function should be monitored at 3 months and 6 monthly thereafter, or more frequently in certain populations (see Assessment of **renal function at baseline**). The management of people with high and ongoing risk of HIV infection, but whose eGFR has declined below or around 60 mL/min/1.73 m2 since commencing TD*/FTC, is challenging. This situation typically requires consultation with a physician who is expert in PrEP. Cessation of TD*/FTC for 1 month may restore eGFR to above 60 mL/min/1.73 m2, following which TD*/FTC may be recommenced with cautious monitoring. In these circumstances, consideration should be given to using on-demand† TD*/FTC, or possibly second-daily TD*/FTC. However, there is no data to show that either of these options will stabilise the eGFR above 60 mL/min/1.73 m2.

Testing for STIs

As PrEP users are at increased risk for STIs **(7)** clinicians should screen for STIs (specifically gonorrhoea, chlamydia and infectious syphilis) every 3 months using the standard-of-care tests and procedures, and manage any detected STI as recommended by the Australian STI Management Guidelines **(1)**. Partner notification should be undertaken using the most appropriate available resources.

It is important to note, that for MSM and other groups where relevant, STI tests must include a throat swab and anal swab for chlamydia and gonorrhoea and vaginal swab should also be taken.

At each follow-up visit, patients taking PrEP should be reminded about:

- prevention of STI acquisition and transmission
- the need for quarterly STI testing
- the need to present for testing and treatment whenever signs or symptoms of an STI appear.

Clinicians should ensure that the pathology service provider that they use has these swabs available.

The presence of an STI at follow-up testing does not prevent the ongoing prescription of PrEP.

Monitoring HBV Hepatitis B and HCV Hepatitis C virus infections

Hepatitis B virus monitoring

For people who are hepatitis B virus (HBV) non-immune at baseline, clinicians should provide hepatitis B vaccination and confirm their immune response 1 month after the last vaccine dose.

For people who state that they have been vaccinated for hepatitis B at baseline, clinicians should test for hepatitis B surface antibody; if their hepatitis B surface antibody is below 10 IU/mL, they should be vaccinated with one dose of hepatitis B vaccine and their hepatitis B surface antibody titre should be checked 1 month later. If their titre does not rise above 10 IU/mL their hepatitis B vaccination should then be completed.

Both TD* and FTC are active against HBV **(8)**. If people living with chronic HBV infection stop taking these medications, hepatic flares can occur, which can be severe **(8)**. Patients with chronic HBV need to be counselled regarding the risks of poor adherence and the risks of self-ceasing PrEP medication. Patients who are known to have chronic HBV and are already taking treatment for this condition should consult their liver specialist before commencing PrEP. A person taking PrEP who has chronic HBV infection should be assessed by a clinician experienced in the management of hepatitis B before ceasing PrEP. If PrEP is discontinued, close monitoring is strongly advised.

Daily PrEP should be offered to people with chronic HBV, on-demand may also be offered under certain circumstances. For additional guidance about the management of PrEP in people with chronic hepatitis B, see **Special clinical considerations**.

Hepatitis C virus monitoring

All people who inject drugs including MSM, trans and gender diverse and heterosexual people should be monitored for Hepatitis C virus (HCV), as should MSM and trans and gender diverse people who engage in sexual contact that may pre-dispose to anal trauma. The incidence of HCV has currently been low at approximately 1% per annum in PrEP studies of MSM **(9, 10)**, and higher in HIV-positive MSM **(11, 12)**. However, there is concern that HCV incidence may increase following changes in sexual and sero-sorting behaviour in the era of PrEP. In this context, HCV can be sexually acquired and is considered as an STI. It should be tested at least annually, and more frequently if necessary, following sexual history taking and review of injecting practices **(13)**.

Managing side-effects

Patients taking PrEP should be assessed for side-effects associated with TD*/FTC use, most importantly those suggesting possible acute renal injury. A review of symptoms experienced in the iPrEx (Iniciativa Profilaxis Pre-Exposición) study showed that potential PrEP-associated symptoms peaked at 1 month, when 39% of participants reported symptoms, compared with 22% at baseline. Gastrointestinal (GI) symptoms occurred in a median of 28% of participants across study sites (range 11–70%) and non-GI symptoms occurred in a median of 24% of participants (range 3–59%). The odds of GI symptoms were higher in those with evidence of high adherence to PrEP. By 3 months, symptoms had returned to pre-PrEP levels **(14)**.

Bodybuilding increases muscle mass, which may result in increased creatinine levels in blood. When evaluating and managing PrEP users with creatinine clearance changes, clinicians should take into consideration the history of steroid, protein, creatine powder use (which also increases blood creatinine levels) and bodybuilding. A wash-out period of 14 days cessation of creatine before renal function assessment may be recommended.

The ASHM PrEP Guidelines Panel will monitor evidence in this area and update the guidelines as appropriate.

Optional assessments

Therapeutic drug monitoring

Initial demonstration projects in Australia conducted therapeutic drug monitoring as part of research protocols to evaluate medication adherence and HIV seroconversions among study participants. Their results revealed a high correlation between self-reports of tablet taking and blood concentrations of TD* and FTC, and high adherence to PrEP (over 90%) **(15, 16)**. However, in Australia there are no clinical laboratories that quantify TD*/FTC concentrations in plasma, cells or urine for therapeutic drug monitoring (TDM) in the setting of PrEP **(17)** and it is likely that therapeutic drug monitoring is likely to be used primarily for research including evaluations of people who acquire HIV infection while taking PrEP.

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Special clinical considerations

Aboriginal and Torres Strait Islander people

The rate of human immunodeficiency virus (HIV) infection is rising in Aboriginal and Torres Strait Islander (hereafter referred to as Indigenous) Australians. Between 2013-2017, the age standardised rate of HIV notifications increased by 41% in Indigenous populations, compared to a 12% decline in Australian-born non-Indigenous people **(1)**. Furthermore, a greater proportion of HIV notifications during 2015-2017 in Indigenous populations was ascribed to heterosexual sex (21%) and injecting drug use (18%), compared to Australian-born non-Indigenous populations (18% and 3%, respectively) **(1)**.

There are few data currently available regarding pre-exposure prophylaxis (PrEP) knowledge, acceptability and use in Indigenous populations. Notably, 2.1% of participants in the Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) study identified as Indigenous **(2)** as did 2.94% in the QPrEPd study in Queensland **(3)**. A recent qualitative analysis examined the obstacles to PrEP use faced by Indigenous men who have sex with men (MSM) **(4)**. These obstacles included individual barriers, such as unwillingness for Indigenous MSM to identify with mainstream gay communities, stigma towards HIV and MSM within Indigenous communities and attitudinal differences towards the use of Western medicine **(4)**. Provider barriers that were identified include overburdened and under-resourced Aboriginal medical services, a perceived lack of confidentiality in these services and a lack of government leadership and funding. Regarding the way forward, many respondents felt community involvement was essential for effective PrEP promotion and that sexual health and PrEP promotion should be better funded and driven by the community. Respondents felt that both mainstream sexual health clinics and Aboriginal Community Controlled Health Organisations can provide appropriate services, although general practitioners, nurses and Indigenous health workers need to improve HIV and sexual literacy **(4)**. Healthcare practitioners must provide an environment that does not stigmatise Indigenous patients. Health-care practitioners must take a careful and culturally appropriate history to ascertain risk factors for HIV infection and PrEP suitability and must provide appropriate treatment and referral to support people who inject drugs.

In 2017, the notification rate of newly diagnosed hepatitis B infection in Indigenous populations was more than double that of non-Indigenous population (45.1 per 100,000 versus 19.2 per 100,000) **(5)**. Given the higher rates of hepatitis B infection in Indigenous versus non-Indigenous people, clinicians caring for Indigenous patients must carefully follow these ASHM PrEP guidelines and screen for hepatitis B infection and, as required, provide hepatitis B vaccinations. People ineligible for Medicare including newly-arrived Asian-born men who have sex with men

People ineligible for Medicare including newly-arrived Asian-born men who have sex with men

Reports during 2013-2017 from a large, sentinel sexual health service in Victoria showed that the proportion of newly-arrived Asian-born MSM with incident HIV infection did not decline whereas the proportion of all other MSM attending the clinic with incident HIV infection declined by 45% **(6)**. At the same clinic during 2017, newly-arrived Asian-born versus all other MSM were less likely to report use of PrEP.

In Australia, access to Medicare is required to receive subsidised PrEP and HIV antiretroviral therapy. People who come to Australia to study who are ineligible for Medicare are required to have Overseas Student Health Cover, however anecdotal reports suggest that some students are reticent to use their private health cover for sexual health testing, prevention and treatment because of concerns about data privacy. People who come to Australia on a Working Holiday Visa (417) may be eligible for Medicare if they come from countries with reciprocal health cover arrangements, although none of these countries is within Asia **(7)**.

Clinicians should refer people who are ineligible for Medicare or who are unable or unwilling to use private health-care cover to public sexual health clinics that offer free HIV and sexually transmissible infection (STI) testing and provide PrEP prescriptions. These PrEP prescriptions can be filled by paying the full, unsubsidised amount for a private script, or by personal importation of PrEP through online pharmacies.

Transgender women

Transgender women have a high prevalence of HIV infection **(8)** and experience high HIV incidence rates compared to non-transgender men and women **(9)**. Furthermore, transgender women have represented less than 1% of study participants in PrEP trials **(10)** and this paucity of data may help explain the overall low uptake of PrEP by transgender women **(11)**.

The Iniciativa Profilaxis Pre-Exposición (iPrEX) clinical trial enrolled the highest number of transgender women to date and found that compared to MSM, transgender women were more likely to report transactional sex, condomless anal intercourse and more recent sexual partners **(12)**. In iPrEX, no HIV infections were observed in transgender women whose blood levels were compatible with taking four or more doses of PrEP weekly. However, using stratified analyses, PrEP did not provide a benefit for transgender women in the iPrEX study [hazard ratio 1.1, 95% confidence interval (CI): (0.5 to 2.7) compared to the overall 44% reduced HIV incidence in the active study arm **(12)**.

A recent retrospective analysis of the iPrEX study sought to determine whether the differential efficacy of PrEP in MSM versus transgender women was a result of different baseline clinical and behavioural factors that could make PrEP less efficacious in transgender women **(10)**. The authors found that baseline characteristics between MSM and transgender women explained almost 100% of the difference in PrEP's efficacy during the iPrEX study **(11)**. However, the authors were not able to comment on whether the use of gender-affirming hormone therapy (GAHT) **(13)** may have contributed to PrEP being less effective in the transgender women study participants **(11)**.

Oestrogen, which is used as part of GAHT, increases the activity of 5'-nucleotidase enzymes and can decrease the active metabolites of tenofovir and emtricitabine, or increase the nucleotides that compete against the active metabolites of tenofovir and emtricitabine within cells. Therefore, oestrogen could plausibly reduce cellular levels of tenofovir and emtricitabine in transgender women, making PrEP less efficacious. There have been some small studies in transgender women taking GAHT and PrEP. One study of 20 Thai transgender women commencing GAHT and PrEP showed a 12% reduction in plasma tenofovir levels in the presence of GAHT **(14)**, although PrEP did not reduce oestrogen levels. In another study, 31% lower levels of plasma tenofovir were observed in eight transgender women taking GAHT compared to eight cis-gender men; plasma emtricitabine was also significantly lower in the transgender study participants **(13)**. A further study compared the rectal tissue levels of the active metabolites of tenofovir and emtricitabine in four HIV-positive transgender women taking GAHT versus four HIV-positive postmenopausal cis-gender women. This study reported that there was a significantly lower ratio of the active metabolite of tenofovir diphosphate to its competing nucleotide dATP in the rectal tissue of the transgender versus cis-gender participants **(15)**. However, this study did not find a decrease in the ratio of the active metabolite emtricitabine triphosphate to its competing nucleotide, dCTP. Further larger pharmacological studies are needed urgently to determine whether GAHT reduces the levels of tenofovir disoproxil* and emtricitabine (TD*/FTC), or vice versa in transgender women.

The ASHM PrEP Guidelines Panel will continue to monitor the data on potential drug-drug interactions between GAHT and TD*/FTC.

As noted, in a post-hoc analysis of transgender women in the iPrEX study, no HIV infections were observed in transgender women whose blood levels were compatible with taking four or more doses of PrEP weekly **(12)**. Therefore, supporting transgender women to optimise their PrEP adherence is important until larger studies have determined whether GAHT reduces levels of TD*/FTC in transgender women taking GAHT. To help support transgender women to optimise their PrEP use and adherence, it is recommended that health practitioners provide gender-affirming care **(16)**. Such clinical care includes appropriate use of preferred pronouns and names, safe access to bathrooms of choice and appropriate treatment and referral for hormone therapy and surgery **(16)**.

Transgender men

There are very few data regarding PrEP knowledge, acceptability and use in transgender men. Nor are there data regarding whether GAHT influences PrEP drug levels or vice versa in transgender men. A 2016 review of HIV and STI research undertaken in transgender men was unable to find any data on the use of PrEP in transgender men **(17)**. In a 2017 study of 181 transgender youth from the USA, of 42 people identifying as transgender men (23.2%), only 16 had ever used HIV prevention services and none had ever used PrEP **(18)**. Transgender men were significantly less likely to have ever used PrEP than transgender women **(18)**. To optimise HIV prevention and PrEP use, clinicians caring for transgender men need to actively raise PrEP as an HIV prevention option for them and take a sensitive and detailed sexual behaviour history bearing in mind that transgender men may be sexually active with male and female partners. Gender-affirming care should be provided to transgender men by health practitioners. For more information see: a language guide: Trans and gender diverse inclusion

Women taking PrEP during conception, pregnancy and breastfeeding

Conception in serodiscordant couples

Women without HIV infection who have sexual partners with documented HIV infection are at risk of HIV acquisition during natural attempts to conceive (i.e. without a condom) if their HIV-positive partner has a detectable or variably detectable plasma viral load. Providers should discuss with their patients the available information about the potential risks and benefits of PrEP in these circumstances **(19)**. For women wanting to conceive where their HIV-positive male partner is stably virologically suppressed on combination antiretroviral therapy (cART), PrEP should still be offered to the woman if she expresses concerns about the risk of acquiring HIV in this setting.

Pregnancy

Among women without HIV infection, the risk of acquiring HIV increases by approximately two-fold during pregnancy **(20)**. In addition, if a woman acquires HIV infection during pregnancy there is a higher risk of HIV transmission to the infant than if the woman were to become pregnant during chronic HIV infection because the HIV viral load is much higher during acute HIV infection.

The current evidence suggests that PrEP can be used safely during pregnancy and breastfeeding **(21)**.

The use of TD*-containing regimens by HIV positive women throughout pregnancy has not been associated with adverse pregnancy outcomes, but lowered BMD has been observed in newborns exposed to TD* in utero **(22)** as has a lower length and head circumference at 1 year of age **(23)**.

In the Partners PrEP study, which compared the efficacy of tenofovir disoproxil fumarate / emtricitabine (TDF/FTC) versus TDF versus placebo to reduce HIV transmission in African heterosexual HIV-serodifferent couples, 431 pregnancies occurred; the average duration of in utero PrEP exposure was 5 weeks **(24)**. There was no difference in the incidence of pregnancy, birth outcomes or infant growth in women who received TDF or TDF/FTC versus placebo PrEP **(24)**. However, the authors noted that the confidence intervals for these findings were wide and therefore definitive statements about the safety of TDF/FTC as PrEP during pregnancy could not be made based on this study's findings. A subsequent study from this group examined the pregnancy outcomes of 30 women who continued to use PrEP during pregnancy compared to 96 pregnancies without PrEP exposure. The authors found that there was no increase in adverse pregnancy outcomes, or restrictions in infant growth between the two groups **(25)**.

The World Health Organization has included PrEP as an HIV prevention strategy during pregnancy **(26)** and a number of other jurisdictions recommend PrEP for safe conception and for use during pregnancy and breastfeeding **(27)**.

Some women with HIV-positive partners may prefer to continue PrEP while pregnant, due to the increased risk of acquisition of HIV if their partners are not reliably virologically supressed during pregnancy, or due to high levels of anxiety **(27)**.

Providers should discuss with their patients available information on potential adverse pregnancy outcomes when beginning or continuing PrEP during pregnancy so that they can make an informed decision. It should be noted that TD* is classified as category B3 by the Australian Therapeutic Goods Administration (TGA) **(29)**, meaning that, to date, tenofovir has been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. However, studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.

Therefore, the ASHM PrEP Guidelines Panel's recommendation is that PrEP may be continued during pregnancy in women at risk for HIV acquisition, or who are unduly affected by anxiety about HIV acquisition.

Breastfeeding

Although experience with PrEP during breastfeeding is lacking, there is substantial experience with the use of TD*/FTC during the breastfeeding period by HIV-positive women taking TD*/FTC based antiretroviral therapy. TD* and FTC are secreted in breast milk, although at much lower concentrations (0.3 and 2%, respectively), of the levels achieved with the doses recommended for the treatment of infants with HIV infection **(30)**. In the PrEP setting, a study evaluating antiretroviral excretion in breast milk and infant absorption suggests PrEP can be safely used during breastfeeding with minimal infant drug exposure **(28)**.

If a woman acquires HIV infection during breastfeeding, the risk of transmission to her infant is higher than in an established infection, because of high viral load soon after seroconversion. Therefore, PrEP can be continued during breastfeeding in women at risk of HIV acquisition.

The ASHM PrEP Guidelines Panel will continue to monitor the safety of TD*/FTC PrEP regimens when used during pregnancy and breastfeeding.

PrEP and Chronic Hepatitis B

The risk of HBV infection is significantly reduced in people who use TD*/FTC for HIV PrEP, with or without HBV vaccination due to these drugs having dual HIV and Hepatitis B activity **(5-7)**.

All people who test positive for hepatitis B surface antigen (HBsAg) should be evaluated for the need for HBV treatment, in accordance with ASHM's guide titled "Hepatitis B for Primary Care" (**https://www.hepatitisb.org.au**). For HIV PrEP prescribers without experience in the evaluation of HBV infection, co-managing the patient with an infectious disease, sexual health, s100 HBV GP, or liver specialist should be considered. However, to improve follow-up, to increase convenience for the patient, and reduce costs for the patient and the health system, the ASHM PrEP Guideline Panel recommend that PrEP monitoring and HBV monitoring should be integrated and performed by the same clinician, at the same visits **(8)**.

Both TD* and FTC are active against both HIV and hepatitis B virus (HBV) infections, but of these two agents, TD* is the only approved agent for treatment of chronic HBV infection in Australia. Although early clinical trials showed that oral TDF by itself is effective as HIV PrEP **(9)**, most subsequent studies have assessed the effectiveness of co-formulated TD*/FTC as HIV PrEP, and hence TD*/FTC PrEP has the most comprehensive evidence base. Also, two case reports describe patients who acquired HIV infection whilst receiving TD* alone for treatment of hepatitis B infection, their tenofovir plasma levels and prescription refills indicating adequate medication adherence.**(10)** **Hence the ASHM PrEP Guideline Panel recommends that people who meet the criteria for treatment of chronic HBV infection and who are at risk of HIV should receive daily co-formulated TD*/FTC.**

Despite previous concerns about the potential for HBV reactivation, hepatitis flares and acute liver failure when PrEP is ceased, emerging data suggests that these outcomes are very uncommon **(11)** hence the PrEP Guidelines Panel endorses the use of TD*/FTC as HIV PrEP in people with chronic HBV infection.

While currently not PBS-listed for this purpose, tenofovir alafenamide (TAF) is also a safe and effective treatment for HBV infection **(12)**. As such, people with HBV infection who require HIV prevention can also use daily oral co-formulated TAF/FTC for PrEP. Of note TAF/FTC is TGA-approved for use as PrEP. TAF/FTC is not PBS-listed for use as PrEP, but it can be purchased across the counter using a private prescription, or be imported through the TGA's self-importation scheme.

Cabotegravir (CAB-LA) has no activity against hepatitis B, and people living with viral hepatitis were excluded from clinical trials of CAB-LA PrEP, hence CAB-LA PrEP is not recommended for people living with hepatitis B.

Use of on-demand HIV PrEP in people with chronic hepatitis B infection

Previously, only daily PrEP was recommended for people living with HBV, due to concerns that on-demand PrEP could result in a hepatitis flare on withdrawal of drugs with hepatitis B activity. With further evidence, the WHO now endorses the use of on-demand PrEP using TD*/FTC for people living with HBV under certain circumstances **(2)**, and the ASHM PrEP Guidelines Panel endorses these recommendations, as outlined below.

Circumstances where on-demand TD*/FTC PrEP can be used for people living with chronic HBV infection

- The person *does not* have cirrhosis of the liver

and/or

- the person *does not require* treatment of HBV infection, e.g. HBV viral load is < 2000 IU and ALT levels are not elevated

In this setting when the person no longer needs to use on-demand PrEP they can cease TD*/FTC, but they should be monitored at 3 and 6 months after ceasing PrEP for evaluation of HBV reactivation

Circumstances where on-demand TD*/FTC PrEP cannot be used for people living with chronic HBV infection

- the person *does have* cirrhosis of the liver

and/or

- the person *requires* treatment of HBV infection e.g. HBV viral load is > 2000 IU and ALT levels are elevated.

If either ALT or HBV VL become elevated during PrEP use or post-PrEP monitoring, advice from an s100 HBV prescriber, sexual health physician, infectious disease physician or gastroenterologist should be sought.

The ASHM PrEP Guidelines Panel recommends that PrEP monitoring and HBV monitoring are performed by the same clinician, at the same visits (8). When PrEP is no longer required, the regimen can be replaced by TD* monotherapy to continue HBV treatment, but the PrEP user needs to understand that future episodes of HIV risk acquisition should be covered by the resumption of TD*/FTC.

Patients with chronic renal failure

Patients without HIV infection and with established chronic renal failure, e.g. with estimated glomerular filtration rate (eGFR) that is stably less than 60 mL/min/1.73 m^2 should not be prescribed PrEP. The only PrEP regimen proven effective to date and approved by the TGA is TD*/FTC, which is not indicated for those with chronic renal failure **(34)**. However, if a patient with chronic renal failure is at substantial risk of HIV, their condition should be discussed with specialists in the management of HIV and renal disease.

Adolescent minors

As a part of primary health care, HIV screening should be discussed with all adolescents who are sexually active, or have a history of injecting drug use. Parental or guardian involvement in an adolescent's health care is often desirable, but is sometimes contraindicated for the safety of the adolescent, and can compromise full disclosure.

Clinicians should carefully consider the data discussed below on the safety and efficacy of daily PrEP taken by persons under 18 years of age, including the possibility of loss of bone mineral density, and other toxicities among youth who are still growing. Data are also available about the safety of TD*/FTC when used in treatment regimens for young people with HIV infection **(35)**. The clinician and the patient may conclude that the short-term, proximal risk of acquiring HIV infection greatly outweighs any short-term, or as yet undetermined, long-term risk of PrEP toxicity. Clinicians are encouraged to seek expert advice in complex situations.

Adherence to PrEP in adolescents may be suboptimal: a PrEP demonstration program involving daily PrEP use for 18–22-year-old HIV-negative MSM reported that tenofovir diphosphate intracellular levels, a marker of cumulative TD* adherence, were consistent with good adherence peaking at 56% at month, but declining thereafter **(36)**. In another open-label 48-week study of 78 adolescent MSM commencing PrEP, Project PrEPare, highly protective levels of PrEP were observed in 54% of adolescents at week 4 but declined thereafter **(37)**.

Following this finding that PrEP levels declined markedly in these adolescent participants after the first week 4 visit, the authors recommended that adolescents should be offered more frequent clinical monitoring to enhance their PrEP adherence. **The ASHM PrEP Guidelines Panel endorses this approach and encourages clinicians to work with adolescents taking PrEP to design an augmented clinical review schedule.**

In the Project PrEPare study, there was no observed elevation in serum creatinine levels and significant increases were observed in bone mineral density for the spine, hip and total body between baseline and week 48 **(37)**. However, there was a slight but statistically significant decline in the total body Z-score during this time **(37)**, suggesting that bone growth may have been suboptimal in the study participants. Although not observed in this study, higher levels of PrEP adherence as measured by red blood cells levels of tenofovir diphosphate have been associated with lower hip bone mineral density in adolescents **(38)**. Further research is needed to determine whether there is a long-term increased risk of bone fractures in young MSM who have had PrEP.

Globally until recently, regulatory approval of Truvada (tenofovir disoproxil fumarate (TDF (FTC)) PrEP was limited to adults over 18 years of age. However, on 15 May 2018, the US Food and Drug Administration (FDA), based on data from the Project PrEPare study discussed above, expanded its approval of Truvada as PrEP against HIV to include adolescents at risk weighing at least 35 kg.

PrEP use for prevention of HIV in adolescents has not been approved by the TGA in Australia. However, clinicians are able to prescribe PrEP off-label for adolescents. In this setting, a decision to prescribe PrEP for a person under 18 years of age should be made at the discretion of the prescriber who is responsible for obtaining informed consent from their patient. Informed consent should take into account the risks and benefits of that treatment versus other available treatments or no treatment at all based on the individual circumstances. Of note, the TGA does not regulate health professionals or clinical practice. Medical practitioners are required to prescribe in accordance with **Good Medical Practice**, the code of conduct published by the **Medical Board of Australia**– this code highlights the importance of informed consent.

Adolescents may obtain PrEP via the Personal Importation Scheme of the TGA once they have received an off-label prescription from their clinician.

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10.

HIV non-occupational post-exposure prophylaxis and pre-exposure prophylaxis

People not receiving human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) who seek care within 72 hours after an isolated sexual or injection-related HIV exposure should be evaluated for the need for non-occupational post-exposure prophylaxis (nPEP) **(1)**. nPEP may also be considered where an individual receiving PrEP reports being poorly adherent and seeks care within 72 hours after an HIV exposure. The clinician should take a sexual history to differentiate isolated exposures from ongoing exposure. If the exposure is isolated (e.g. an isolated condom failure, sexual assault), nPEP should be prescribed, but ongoing antiretroviral medication is not indicated after completion of the 28-day nPEP course.

If exposures are not isolated but ongoing, clinicians should consider offering PrEP immediately. If the person needs a three-drug nPEP regimen, the nPEP should be prescribed initially and then the individual should be supported to transition to PrEP.

The decision to commence nPEP should be made according to local nPEP guidelines **(1)**. The decision to transition to PrEP is dependant upon suitability for PrEP (including a confirmatory negative HIV test result) and the individual's willingness to continue taking daily tenofovir disoproxil* and emtricitabine (TD*/FTC) and to attending quarterly clinic visits whilst on PrEP.

For a person already using PrEP, a course of nPEP may be required if the PrEP user had a recent high-risk exposure (within 72 hours) and did not take PrEP during the period that the high-risk exposure occurred. The decision to recommence PrEP following a course of nPEP is dependent upon the individual's ongoing eligibility for PrEP (including a negative HIV test result) and their willingness to continue taking daily TD*/ FTC.

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11.

Improving medication adherence

Medication adherence is critical to achieving the maximum prevention benefit of preexposure prophylaxis (PrEP) and reducing the risk of selecting for a drug-resistant virus in the event of human immunodeficiency virus (HIV) acquisition **(1, 2)**. In randomised, blinded, placebo-controlled trials of PrEP, adherence varied **(1)** and was lower among cisgender women in some studies **(3, 4)**, in transgender women **(5)** and young PrEP users **(6-8)**. PrEP adherence has generally been higher in more recent trials, open-label extensions and demonstration projects, particularly among men who have sex with men (MSM). These better adherence rates have been due to increasing knowledge about PrEP's efficacy and differing motivations for taking PrEP **(1, 9-12)**.

Common reasons for non-adherence include a perceived low risk of acquiring HIV **(3, 4, 13)**, start-up symptoms **(3, 14-16)** and concerns regarding long-term side-effects **(13, 17)**, factors of daily life such as memory (forgetting and being unsure whether the dose was taken) and medication management **(18, 19)**, perceived and enacted stigma due to being eligible for PrEP **(19-22)** and lack of social support from partners, family and friends **(19)**. Common challenges to PrEP adherence, particularly for MSM, are party drug and alcohol use **(18)**. Party drug use (at the event level) is known to increase the likelihood of missing a dose on the same as well as the next day, thus potentially impacting on the efficacy of event-driven PrEP **(23)**. People with mental health disorders are also more likely to self-discontinue the use of PrEP **(24)**. For some patients, the cost of medical appointments (where not bulk billed) and dispensing fees are a big deterrent to PrEP adherence. Studies of adolescent MSM using PrEP have shown that approximately 55% of participants have evidence of high adherence at week 4, but adherence declines markedly after the first month **(7, 8)**.

Patient education and adherence counselling focused on medication self-management are needed to support ongoing daily PrEP use (Box 11.1).

BOX 11.1 KEY COMPONENTS OF MEDICATION-ADHERENCE COUNSELLING

Establish trust and bidirectional communication

Provide simple explanations and education on the following issues:

- Relationship of adherence to the efficacy of PrEP
- Medication dosage and schedule
- Management of common side-effects
- Signs and symptoms of acute HIV infection and recommended actions.

Support adherence:

- Tailor daily dose taking to patient's daily routine (a fixed time for dosing, e.g. in the morning, with tooth brushing, before bed)
- Identify reminders and devices (e.g. beepers, alarms widely available over the counter) to minimise forgotten doses
- Identify solutions for patients unable to attend three-monthly clinical visits
- Identify back-up mechanisms (e.g., pill stashing and pocket doses) for those times when a dose is forgotten.
- Identify and address potential barriers to adherence.

Monitor medication adherence in a non-judgmental manner:

- Normalise occasinal missed doses while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address these factors
- Assess side-effects and provide advice on how to manage them.

Various approaches can be used to effectively support medication adherence (25). These include:

- educating patients (including population groups other than MSM particularly women who may be considering PrEP) about the medications
- helping patients anticipate and manage side-effects
- helping patients establish dosing routines that fit with their work and social schedules
- providing reminder systems and tools such as pill boxes and electronic reminders
- addressing substance abuse or mental-health needs that may impede adherence
- arranging more frequent clinic visits for adolescents to enhance their adherence
- facilitating social and peer support, especially for women.

When initiating a PrEP regimen, clinicians need to educate patients about medication schedules (for daily or on-demand† PrEP, that is, the use of PrEP before and after potential HIV exposures), how to commence taking PrEP and how to cease taking PrEP and what to do if they experience problems such as side-effects or missed doses. See section **Providing PrEP** regarding specific recommendations about dealing with missed doses.

Medication adherence should be discussed at each visit when the PrEP script is provided to identify barriers to optimal PrEP adherence and develop appropriate management plans. Real-time, bi-directional mobile phone contact/access to clinic staff (commonly by SMS) can be useful for patients experiencing side effects, missing doses and those with complex needs.

Emerging evidence that different dosing strategies can be effective provides an opportunity to offer flexibility, choice and convenience to patients who are benefiting from PrEP. On-demand† PrEP is now an option for suitable patients as endorsed in guidance from the World Health Organization **(26)** (see Providing PrEP). If patients choose to take on-demand† PrEP, their behaviour and PrEP pill use patterns should be discussed at each visit, to help determine if they should perhaps switch to daily PrEP.

Side-effects can lead to non-adherence. Clinicians should inform patients about the most common side effects and should work with patients to develop a specific plan for handling them, including the use of specific over-the-counter medications that can mitigate symptoms.

In the context of discussing PrEP adherence, patients should be reminded about the need to be tested for HIV and sexually transmissible infections (STIs) every 3 months or earlier if required, due to perceived risks or symptoms.

The importance of using condoms to prevent STIs, or to help prevent HIV if PrEP adherence has been suboptimal should be discussed with patients. To improve adherence and effectiveness of PrEP, patients should also be informed about, how to stop taking PrEP and re-start it, so that they are prepared to these changes in advance - See section providing PrEP regarding specific recommendations on **starting and ceasing PrEP**.

Clinicians may wish to explore and address other potential barriers to optimised PrEP use such as misconceptions about PrEP, behavioural factors (e.g. substance use), depression, partner violence and unstable housing. To improve adherence to their PrEP medication, some patients may need referral to mental health or social services, or peer-based support services provided by various organisations (e.g. services provided by Living Positive Victoria and Positive Women Victoria, or similar groups in other Australian jurisdictions to support families and serodiscordant couples).

† The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.

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12.

Behavioural strategies to reduce risk

In the era of human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) and treatment as prevention, behavioural methods of risk reduction – including condom use, clean injecting equipment, HIV serosorting, strategic positioning, and negotiated safe practices with sexual partners– retain their importance in preventing HIV transmission (Box 12.1). However, some vulnerable individuals, particularly some cis-gender and transgender women, may be unable to effectively negotiate use of these prevention strategies, especially condoms, with their regular, or casual partners. The initiation of PrEP is straightforward, but on occasion it may be appropriate to refer some particularly vulnerable people with complex needs to health professionals with expertise in HIV prevention and sexual health.

PrEP's efficacy relates directly to the patient's adherence to PrEP medication not to whether the patient is using condoms in tandem with PrEP **(1,2)**. Individuals should be supported with ongoing information about the role that condoms and other practices play in preventing HIV when PrEP adherence is sub-optimal as well as the role that condoms play in sexually transmissible infection (STI) prevention.

BOX 12.1 DISCUSSION POINTS ON BEHAVIOURAL REDUCTION OF HIV AND STI RISK.

Provide feedback on HIV risk factors identified during sexual and substance use history taking:

- Elicit barriers to, and facilitators of consistent condom use and other safer sex and substance use practices
- Elicit barriers to, and facilitators of, reducing injecting drug use
- Discuss with patients the barriers to, and facilitators of, evidence-based drug treatment where indicated and requested.

Support risk-reduction efforts:

- Help patients identify one or two feasible, acceptable, incremental steps toward risk reduction
- Identify and address anticipated barriers to accomplishing planned actions to reduce risk.

Monitor medication adherence in a non-judgmental manner:

- Acknowledge the effort required for behavioural change
- Reinforce success.

If not fully successful, assess factors interfering with completion of planned actions and help patient identify the next steps (including consideration of commencing PrEP).

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13.

How to access PrEP in Australia

There are three ways to access HIV pre-exposure prophylaxis (PrEP) in Australia:

1.Through the Australian health-care system

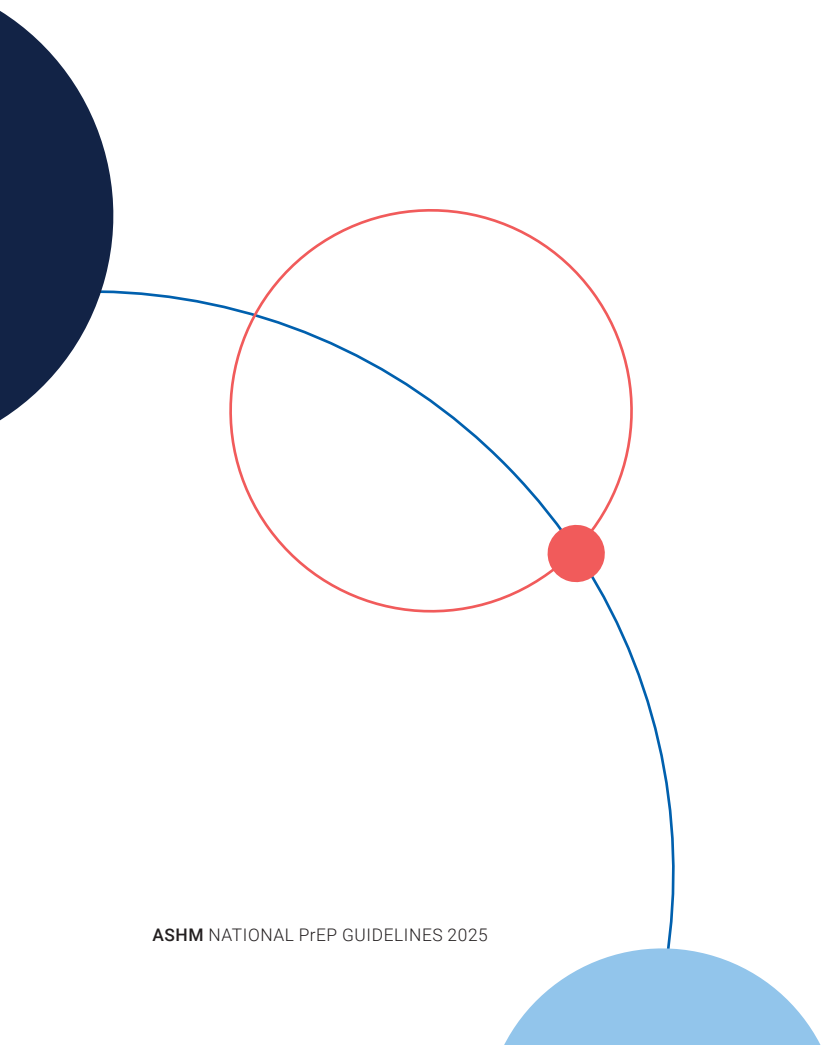
For an Australian resident with a current Medicare card, PrEP can be accessed through the Pharmaceutical Benefits Scheme (PBS) at a subsidised cost. As PrEP is listed as a Schedule 85 (s85) drug, any doctor or authorised nurse practitioner can write a script for PrEP which can be taken to any pharmacy for dispensing. If PrEP is accessed in this way, a PBS co-payment at the pharmacy will need to be made.

2. Private script for supply from Australian pharmaceutical manufacturer

Any doctor or authorised nurse practitioner can write a private script for PrEP and they have three brands to choose from (currently Gilead Sciences Pty Ltd, Generic Health Pty Ltd, Apotex Pty Ltd and Alphapharm Pty Ltd). Patients can have this script dispensed at a community pharmacy. The cost for a private script is higher than for PBS-subsidised medicines. This option is generally used by people who are not eligible for Medicare and who do not feel comfortable using the Personal Importation Scheme described below.

3.Through personal importation or purchase

If a person is not eligible to access PrEP through Medicare, or finds the cost of purchasing PrEP locally too high, then another option is to purchase a generic version of the drug online from a reliable overseas supplier using the Therapeutic Goods Administration's Personal Importation Scheme. A script from a doctor is still required before ordering online. There are multiple overseas suppliers who will supply PrEP for import into Australia at a range of costs. **The PrEP Access Now** website has more information on personal importation.



14.

Models of PrEP delivery in clinical practice

Since 2016, many accredited prescribers of s100 HIV medication, sexual health specialists, general practitioners (GPs), nurse practitioners, nurses in New South Wales, Queensland, Victoria, South Australia, Tasmania, Western Australia and the Australian Capital Territory have been involved in making pre-exposure prophylaxis (PrEP) available through clinical PrEP implementation trials and people self-importing PrEP. Since 1 April 2018, tenofovir disoproxil* and emtricitabine (TD*/FTC) and its generic versions have been available in Australia for human immunodeficiency virus (HIV) PrEP at subsidised cost and can be prescribed through the Pharmaceutical Benefits Scheme (PBS) by any GP or specialist **(1)**.

Making PrEP easily accessible to all Australians where they live requires local medical practitioners and authorised nurse practitioners to be aware of, and comfortable with prescribing, PrEP. Therefore, GPs' knowledge, acceptance and ability to provide PrEP are instrumental to optimising PrEP access and use.

ASHM's Online Learning Module: **Introduction to PrEP Prescribing** as well as other PrEP resources for clinicians are designed to upscale their knowledge and skills: PrEP resources.

The prescription and provision of PrEP clinical and laboratory monitoring are straightforward for GPs and other clinicians. However some providers who are less experienced in serving populations at high risk of acquiring HIV and sexually transmissible infections (STIs) (e.g. men who have sex with men, transgender and gender-diverse people, Indigenous Australians, women involved in sex work, people whose partners are at high risk for HIV/STI, and people who inject drugs) may wish to consider establishing relationships with experienced and accredited HIV s100 prescribers, HIV clinics and sexual health centres, that can provide information and support if required and may be able to do so via Telehealth. Initiatives such as telementoring **(2)** and innovative Information and Communication Technology (ICT) solutions offered by eHealth NSW **(3)** are good examples of how communication technologies can support new PrEP prescribers in remote areas where traditional sexual health services may be limited.

When starting PrEP services, providers should also establish:

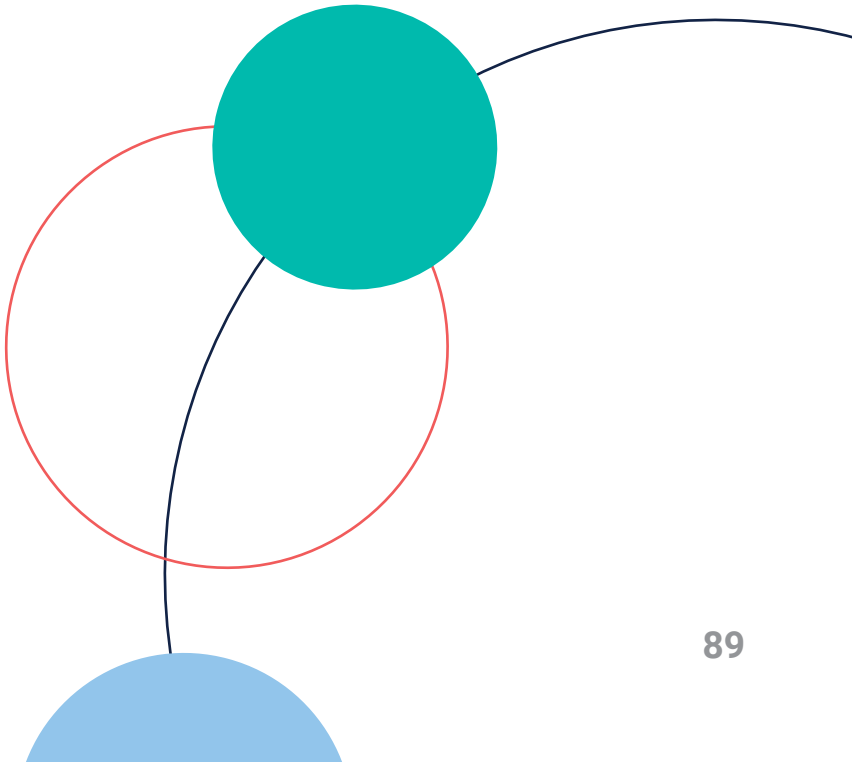
- Appropriate referral pathways to ensure that specific needs of PrEP users are adequately provided (e.g. regular HIV and STI testing, the management of chronic hepatitis B infection, treatment of hepatitis C and possible abnormal liver and kidney function – see **Clinical Assessment** for more details.
- Communication with local pharmacies to ensure uninterrupted refills of PrEP scripts. In rural and remote Australia, clinicians are advised to establish pathways with clinicians and pharmacies in metropolitan areas to help provide clinical support and provide an uninterrupted postal supply of PrEP medications.

An important approach to successful PrEP implementation is to engage representatives from HIV community-based organisations working with relevant populations in the delivery of PrEP (see Resources page for Australia's State and Territory-based AIDS Councils). AIDS Councils can assist with PrEP promotion and education and, depending on their capacity, may also be able to assist with behavioural screening and adherence support. Similarly, support can be useful from community-based organisations working with culturally diverse communities, to ensure equality of access to PrEP.

When embarking on PrEP prescribing, providers should also consider the capacity of their practices to accommodate new patients and maintain follow-up every 3 months while taking PrEP. Several approaches may be helpful in dealing with these changes to practice:

- Careful planning of clinic appointments to allow sufficient space for PrEP initiation and regular follow-up visits
- Where resources allow, automating most steps in the patient pathway, to reduce the patient registration-to-PrEP prescription time
- Task shifting including having clinical nurse specialists, or trained nurses with clinician supervision in charge of PrEP-related services where possible
- Developing systems and procedures for recording and monitoring PrEP use.

Finally, clinical practices that are planning to build up their PrEP patient population can consider developing a customised communications plan for PrEP demand creation, including media channels and communication strategy which will be used to drive local PrEP awareness and use, with input from relevant local community-based organisations and sexual health services.



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15.

Suitability for PrEP – Parallel of Chapter 4

The guidance on PrEP suitability in this chapter is identical to the guidance provided in Chapter 4 on PrEP suitability. However this chapter is written for clinicians who prefer to and are skilled in evaluating people's suitability for PrEP according to how the person reports their gender identity and sexuality. For example a person assigned female at birth may identify as male (trans male) and their sexuality as a man who has sex with men (MSM). In this setting, the clinician would know to evaluate the person's suitability for PrEP based on the possibility that the person may practice both vaginal and anal sex. Alternatively a person assigned male at birth may identify as female (trans female) and their sexuality as heterosexual. If this person has undertaken gender-affirming surgery the clinician would then know to evaluate the person's suitability for PrEP based on the possibility that the person may practice both vaginal and anal sex. This Parallel of Chapter 4 foreshadows a future where all clinicians will be able to skilfully and comfortably evaluate the sexual health of their patients based on how their patients identify their gender and sexuality. For more information see: **A Language Guide: Trans and Gender Diverse Inclusion**.

Pre-exposure prophylaxis (PrEP) medications are registered in Australia with the Therapeutic Goods Administration (TGA) and they are subsidised by the Australian Pharmaceutical Benefits Scheme (PBS). All general practitioners and other medical specialists can prescribe PrEP using a PBS streamlined authority arrangement. No specialist training is required to prescribe PrEP, however resources and training guidance are available for clinicians who are new to prescribing PrEP.

People presenting for PrEP are typically at high risk of human immunodeficiency virus (HIV) infection and they should not be dissuaded from using PrEP. To do so is to deny a person access to one of the most effective HIV prevention tools currently available. Doctors and authorised nurse practitioners who are not comfortable prescribing PrEP should refer the patient immediately to a colleague, or another service that does provide PrEP.

It should also be highlighted that sexual history taking is a necessary and routine part of medical practice, and when this process identifies that a patient may be at risk of HIV, clinicians should proactively offer these patients PrEP. Furthermore clinicians are encouraged to raise PrEP as an HIV prevention strategy with patients whom they perceive to be at risk of HIV infection, even if the purpose of the patient's visit is not related to sexual health, sexually transmissible infections (STIs) or drug use.

These ASHM 2025PrEP guidelines recommend daily PrEP for all people at risk of HIV infection. In addition, these guidelines also recommend that on-demand† PrEP should be offered as an alternative option to suitable patients. Please refer to section **Providing PrEP** for further information on initiating PrEP.

PrEP providers need to obtain a thorough sexual and drug-use history at baseline to determine a person's suitability for PrEP and to review their ongoing need for PrEP at each 3-monthly clinical review. It is important to acknowledge that a person's behaviour may change over time, and that a person may wish to continue PrEP even if their current HIV acquisition risk is not high.

These guidelines acknowledge that PrEP should be recommended as an HIV prevention strategy for people who have been at risk of HIV infection during the previous 3 months and who foresee having similar risks in the next 3 months. These guidelines also recommend PrEP for people who have not been at risk of HIV infection during the previous 3 months, but whose circumstances have changed, and they foresee HIV risk occurring in the next 3 months.

Please note that people who are eligible for PrEP based on their sexual behaviour may be simultaneously eligible for PrEP based on their injecting and other drug use behaviour and vice versa.

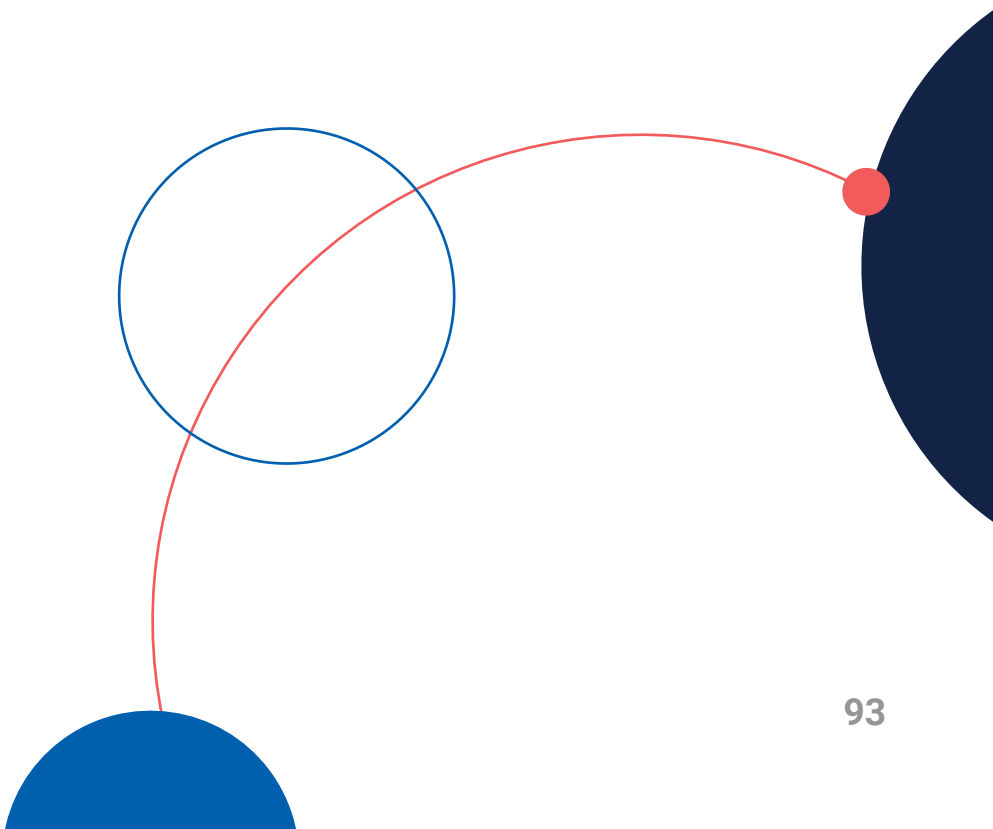
The following suitability criteria can be used to help structure a discussion with a patient about their sexual health and behaviour. Guidance on how to initiate and guide a discussion about a person's sexual and drug using behaviour in primary practice is available **(1)**.

Only a small proportion of participants in PrEP studies have been transgender (trans) or gender diverse people (2, 3, 4). As a result, limited data are available for these populations. Incorrect assumptions can be made about trans people and their sexual practices, as they may practice vaginal/neovaginal and anal intercourse, both insertive and receptive. Trans and gender-diverse people who are at risk of acquiring HIV on the basis of their sexual history are eligible to access PrEP. It is essential for clinicians to take a sexual history using appropriate and sensitive language to assess risk.

Clinicians who have limited experience with prescribing PrEP are encouraged to discuss with a PrEP experienced clinician those patients whose PrEP suitability is unclear.

PrEP suitability criteria for men who have sex with men

This section addresses PrEP suitability for MSM. This section is relevant to people who were assigned male at birth and identify as male, known as cis men. This section is also relevant to people who were assigned female at birth but identify as male, known as trans men. Of note, tran -men who have sex with men may practice both anal and vaginal sex.



BOX 15.1 PREP SUITABILITY CRITERIA FOR MEN WHO HAVE SEX WITH MEN

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months:

- At least one episode of condomless anal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive condomless anal intercourse with any casual male partner
- At least one episode of condomless receptive vaginal sex with a regular HIV+ partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive condomless vaginal sex with any casual HIV+ male partner, or a male partner whose HIV status is unknown
- More than one episode of vaginal sex where a condom slipped off or broke where the HIV serostatus of the partner was not known, or where the partner was HIV+ and not on treatment or had a detectable viral load on treatment
- One or more episodes of engaging in sexualised drug use, sometimes referred to as 'chemsex'. In the Australian context this typically involves the use of crystal methamphetamine (Ice), but can also include the use of gamma hydroxybutyrate (GHB)
- One or more episodes of rectal/vaginal gonorrhoea, rectal/vaginal chlamydia, or infectious syphilis, including any STIs diagnosed at screening for PrEP
- More than one episode of anal intercourse where a condom slipped off or broke where the HIV serostatus of the partner was not known, or where the partner was HIV positive and not on treatment or had a detectable viral load on treatment.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months.

Note: The following list is not exhaustive and there are likely to be many other scenarios where PrEP could be suitably offered for people whose HIV risk acquisition is exclusively in the future:

- When a person plans to travel during which time they anticipate that they will be having condomless sex with casual partners
- When a person plans to return home to an overseas country which has a high HIV prevalence during which time they anticipate that they will be having condomless sex with casual partners
- When a person reports that they have recently left a monogamous relationship and will be having condomless sex with casual partners in the future
- When a person reports that they will be entering or leaving institutional or correctional facilities in the near future where they may have condomless sex with casual partners in the future
- When a person presents with concerns of deteriorating mental health and a history of having previously increased their HIV acquisition risk behaviour in this setting
- When a person presents with a history of intermittent binge drinking of alcohol or recreational drug use and a history of having had increased their HIV acquisition risk behaviour in this setting.

The clinician should consider prescribing PrEP also in the following circumstances:

- When an HIV serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment
- When a person reports being so anxious about HIV infection that it may prevent them from having regular HIV testing, or engaging in any form of anal sex
- When a person presents with a history of recurrent genital ulceration or dermatoses (e.g. psoriasis), as this may increase the risk of HIV transmission.

PrEP suitability criteria for heterosexuals

This section addresses PrEP suitability for heterosexuals. This section is relevant to the following populations: (i) people who were assigned female at birth, identify as female and as heterosexual; (ii) people who were assigned male at birth, identify as male and identify as heterosexual; (iii) people who were assigned male at birth, identify as female (trans female) and identify as heterosexual and (iv) people who were assigned female at birth, identify as male and identify as heterosexual.

BOX 15.2 PREP SUITABILITY CRITERIA FOR HETEROSEXUALS

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months.

- At least one episode of condomless anal or vaginal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive anal or vaginal condomless intercourse with any casual HIV-positive partner or a male bisexual partner of unknown status
- Episodes of planned condomless insertive or receptive vaginal sex in an effort to conceive with an HIV-positive partner, regardless of the HIV-positive partner's viral load.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months:

- Future episodes of planned condomless insertive or receptive vaginal sex in an effort to conceive with an HIV-positive partner, regardless of the HIV-positive partner's viral load
- When a person plans to travel to countries with high HIV prevalence during which time they anticipate having condomless sex with casual partners who are HIV positive or of unknown HIV serostatus
- When a person plans to return home to an overseas country which has a high HIV prevalence during which time they anticipate that they will be having condomless sex with casual partners
- When a person reports that they have recently left a monogamous relationship and will be having condomless sex with a casual HIV positive partner, or a male or female partner of unknown HIV serostatus from a country with high HIV prevalence, or a male partner who is thought to have sex with men
- When an individual reports that they will be entering, or leaving institutional or correctional facilities in the near future where they may have condomless sex with HIV+ or gay or bisexual male casual partners in the future
- When a person presents with concerns of deteriorating mental health and a history of having had increased their HIV acquisition risk behaviour in this setting
- When a person presents with a history of intermittent binge drinking of alcohol or recreational drug use and a history of having had increased their HIV acquisition risk behaviour in this setting.

The clinician should consider prescribing PrEP also in the following circumstances:

- When an HIV serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment.

PrEP suitability criteria for people who inject drugs

In the first instance, people who inject drugs (PWID) should be advised of and provided with options for using sterile needles, syringes and other injecting equipment, and offered opioid substitution therapy for those who use opioids. People who inject drugs can be referred to local needle and syringe programs, or the **Australian Injecting and Illicit Drug Users League** affiliates in their state or territory.

Because PWID are susceptible to a range of infections and injuries, PrEP and other HIV-prevention interventions should be integrated into prevention and clinical care services for hepatitis A, B and C infection and other infectious diseases, and overdose prevention. These interventions include screening for hepatitis A, B and C viruses and providing incentivised vaccination for hepatitis A and B where clinically indicated, as well as screening for injection-related injuries and infections including abscesses, septicaemia and endocarditis **(5)**.

The ASHM PrEP Guidelines Panel is cognisant of the concerns of the International Network of People who Use Drugs. The Network cautions against prioritising PrEP at the expense of other proven interventions as the prime HIV-prevention strategy for people who inject drugs, and emphasises that access to harm reduction services remains a critical component of HIV prevention in people who inject drugs **(6)**. This approach is particularly relevant in Australia where sterile needle and syringe coverage is high and HIV prevalence and incidence among people who inject drugs remains low and stable **(7, 8)**. A recent systematic review of HIV-treatment adherence among PWID in the United States and Canada, undertaken to inform potential PrEP adherence interventions for people who inject drugs, found that younger age, female sex, homelessness and incarceration were obstacles to HIV treatment adherence **(9)**. By comparison, self-sufficiency, use of opioid substitution therapy, and high quality patient-provider relationships were facilitators for adherence **(9)**. Self-reports from HIV-negative people who inject drugs were that HIV–related stigma in social networks, negative experiences with health-care providers, lack of money, homelessness and the criminal justice system were likely barriers to PrEP access **(10)**. These factors should be considered when providing support to people commencing PrEP when they are at risk of HIV through injecting drug use.

The ASHM PrEP Guidelines Panel will continue to monitor the outcomes of the few ongoing studies of HIV PrEP in PWID.

BOX 15.3 PREP SUITABILITY CRITERIA FOR PEOPLE WHO INJECT DRUGS

HIV risk in the previous 3 months and the future 3 months

The clinician should prescribe PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months and if the patient foresees that there are likely to be similar acquisition risks in the next 3 months:

- Shared injecting equipment with an HIV-positive person or with a gay or bisexual man of unknown HIV status
- At least one episode of condomless anal or vaginal intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load
- At least one episode of receptive anal or vaginal condomless intercourse with any casual HIV-positive partner or a male homosexual or bisexual partner of unknown status.

HIV risk in the future 3 months

The clinician should prescribe PrEP if the patient foresees that they will have HIV acquisition risk in the upcoming 3 months, despite not having had HIV acquisition risk in the previous 3 months.

- A person has recently (re)commenced injecting drugs and is injecting with a person who is HIV positive, or with a gay or bisexual man whose HIV status is unknown
- When a person plans to travel to countries with high HIV prevalence during which time they anticipate injecting drugs with other people who are HIV positive or of unknown HIV serostatus
- When a person reports that they will be entering, or leaving institutional or correctional facilities in the near future during which time they may inject drugs with people who are HIV positive or of unknown HIV serostatus

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Appendix 1

PrEP Tool. Electronic version downloadable from: https://ashm.org.au/resources/decision-making-in-prep/

Prescribing Oral HIV Pre-Exposure Prophylaxis (PrEP) in Australia

HIV

PrEP can be prescribed by all medical practitioners and nurse practitioners using PBS scripts. No specialist training is required.

1 BEHAVIOURAL SUITABILITY

Patient requests PrEP

Proceed to step 2

Patient unsure whether to start PrEP
OR
HIV risk identified during consultation

Refer to Table 1. HIV Risk

- Low or no HIV risk → **PrEP may not be indicated.** Discuss alternative HIV risk reduction methods
- HIV risk → Proceed to step 2

2 CLINICAL SUITABILITY

Confirm HIV status and review medical history including renal function

- **HIV Negative** (ideally within the last 7 days but for people who cannot easily access HIV testing, within the past 4 weeks)
  - Assess clinically for acute HIV infection (e.g. fever, night sweats, fatigue, myalgia, arthralgia, rash, headache, pharyngitis, generalised lymphadenopathy, diarrhoea)
  - **Confirm renal function:**
    - **eGFR:** at least 30mL/min → Exclude use of nephrotoxic medication (e.g. high-dose NSAIDS) or medications that interact with PrEP. See Liverpool HIV Drug Interactions Checker → Proceed to Step 3
    - **eGFR:** below 30mL/min → Not for PrEP
- **HIV Negative** But recent HIV exposure (within 72 hours)
  - **Immediately seek advice** on the need for Post- Exposure Prophylaxis (PEP). PEP must be started no later than 72 hours after the exposure - ideally within 24 hours. Refer to ASHM PEP Guidelines
  - Plan to commence PrEP upon completion of PEP course → Repeat step 2
- **HIV Positive** → Not for PrEP. Refer to an HIV s100 Prescriber for treatment. See ASHM HIV Prescriber map

3 OTHER TESTING

Assess for STIs and viral hepatitis

Test	Advice
Hepatitis A serology	Vaccinate if non-immune
Hepatitis B serology (HBsAg, Anti-HBs, Anti-HBc)	• Vaccinate if non-immune • Confirm immune response 1 month after last vaccine dose • If HBsAg+ve, refer to HBV specialist/ prescriber See ASHM HBV Prescriber map
Hepatitis C serology (anti- HCV; followed by HCV RNA if anti- HCV +ve)	If HCV RNA+ve, then treat.See ASHM Decision Making in HCV tool
STIs (i.e. syphilis, gonorrhoea, chlamydia)	As per Australian STI Management Guidelines
Pregnancy test	For people with childbearing potential

Proceed to step 4

4 PRESCRIBING PREP

Choose dosing schedule

Daily continuous PrEP

Suitable for anyone with an ongoing risk of HIV. Start 7 days before HIV risk exposure

Prescribe: tenofovir disoproxil 300mg + emtricitabine 200mg (coformulated); 1 pill daily, Qty 30, Rpt 2
Note: patients with eGFR between 30 - 60mL/min are only suitable for PrEP as tenofovir alafenamide + emtricitabine

Ongoing monitoring (see Table 2 next page)

OR

On Demand PrEP* (2-1-1 method)

Suitable only for: people assigned the male sex at birth with HIV risk from sexual exposure, who also:
- are NOT using exogenous oestradiol-based hormones
- do NOT have chronic HBV with liver cirrhosis
- do NOT require treatment of HBV infection
- do NOT have renal impairment (eGFR 30 - 60mL/min)

Prescribe: tenofovir disoproxil 300mg + emtricitabine 200mg (coformulated); Qty 30, Rpt 2
Dosing:
- 2 pills 2-24 hours before sex
- 1 pill 24 hours later
- 1 pill 48 hours after first dose

If repeated sexual activity, then continue with 1 pill daily until 48h after last sexual contact

Ongoing monitoring (see Table 2 next page)

Notes on prescribing PrEP

- PrEP can be initially prescribed on the same day as a HIV test. Patient to be advised to commence PrEP within 7 days of their HIV test.
- PrEP is PBS-listed for patients who have either (i) a negative HIV test result no older than 4 weeks, (ii) evidence that an HIV test has been conducted, but the result is still forthcoming
- PBS Restricted Benefit
- Patients not eligible for PBS subsidised PrEP can be assisted to import PrEP under the TGA's self importation scheme, on a private prescription – www.pan.org.au

*** The Therapeutic Goods Administration (TGA) has not approved this regimen in Australia.**

This guidance is based on the ASHM's National PrEP Guidelines prepguidelines.com.au.

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TABLE 1. HIV RISK

A person is considered to be at risk of HIV if they had any of these risks in the past 3 months, or if they foresee these risks in the upcoming 3 months.

However, this list is not exhaustive, and patients who do not report these circumstances may still benefit from PrEP.

If a partner is known to be living with HIV, on antiretroviral treatment and has an undetectable viral load, then there is no risk of sexual HIV transmission from this partner.

Men who have sex with men (MSM) and trans & gender diverse people	Heterosexual people
• Receptive condomless intercourse with any casual male partner • Regular condomless intercourse with a person living with HIV who is not on treatment and/or has a detectable viral load • Rectal gonorrhoea, rectal chlamydia or infectious syphilis • Shared injecting equipment with with a person living with HIV or with MSM of unknown HIV status	• Receptive condomless intercourse with any casual MSM partner • Regular condomless intercourse with a person living with HIV who is not on treatment and/or has a detectable viral load - this includes planned natural conception • Shared injecting equipment with with a person living with HIV or with MSM of an unknown HIV status

PATIENT EDUCATION

Discuss:
- The role of condoms and regular STI testing in STI prevention
- Safer injecting practices, if applicable PrEP adherence at every visit
- The requirement for ongoing monitoring every 3 months
- Potential side effects, early (e.g. headache, nausea) and longer term (e.g. renal toxicity, lowered bone density)
- Nephrotoxic medications, e.g. NSAIDs

STOPPING PrEP

- Only cisgender men and other people assigned male at birth not taking exogenous oestradiol-based hormones, taking daily or on-demand PrEP, can stop 48 hours after last exposure
- Other patients on daily PrEP should continue PrEP for 28 days after last exposure
- Patients who stop PrEP need a plan to restart PrEP if their HIV risk increases again

ONGOING MONITORING
TABLE 2: CLINICAL FOLLOW-UP OF PATIENTS WHO ARE PRESCRIBED PREP

Test	Approx. 30 days after PrEP initiation (optional but recommend in some jurisdictions)	90 days after initiating PrEP	Every subsequent 90 days on PrEP	Other frequency
HIV testing & assessment for signs or symptoms of acute infection	✓	✓	✓	
Assess PrEP side effects	✓	✓	✓	
eGFR		✓		✓ at least every 6 months or according to risk of CKD
Urine protein creatinine ratio (PCR) baseline		✓		✓ every 6 months
Hepatitis C serology				✓ 12 monthly but, more frequently if ongoing risk e.g. non- sterile injection drug use and MSM with sexual practices that predispose to anal trauma
Hepatitis B serology				✓ if patient required hepatitis B vaccine at baseline, confirm immune response 1 month after last vaccine dose
STI testing (i.e. syphilis, gonorrhoea, chlamydia)		✓	✓	
Pregnancy test (for people with childbearing potential)		✓	✓	

 ISBN: 978-1-921850-97-4.

This guidance is based on the ASHM's National PrEP Guidelines prepguidelines.com.au.

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Appendix 2

Cockcroft–Gault formula

eCrClCG=[[(140−age)×IBW×0.85 for females]÷(serum creatinine×72)]

IBW=ideal body weight

Males: IBW=50 kg+2.3 kg for each inch over 5 feet

Females: IBW=45.5 kg+2.3 kg for each inch over 5 feet, age in years, weight in kg, and serum creatinine in mg/100 mL

Optional adjustment for low actual body weight [2]

If the actual body weight is less than the IBW use the actual body weight for calculating the eCrCl.

Optional adjustment of high actual body weight [2]

Used only if the actual body weight is 30% greater than the IBW. Otherwise, the

IBW is used. eCrCl=[[(140−age)×AjBW]÷(serum creatinine×72)] (×0.85 for females)

AjBW=IBW+0.3(ABW−IBW)

AjBW=adjusted body weight; ABW=actual body weight

Optional adjustment for body surface area (BSA) [3]

Can be used if actual body weight is greater or less than IBW eCrClBSAadj=1.73 m2×eCrClCG (mL/min)÷BSA of the patient (m2)

BSA (DuBois and DuBois formula [4])=(height (m) 0.725×weight (kg)

0.425)÷139.2

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Appendix 3

Current list of TGA Approved HIV diagnostic and monitoring tests on the Australian Register of Therapeutic Goods (as of May 2019).

1. **Roche Diagnostics Australia Pty Limited - cobas HIV-1/ HIV-2…**
   ARTG ID: 313870
   Product name: cobas HIV-1/HIV-2 Qualitative - HIV1/HIV2 nucleic acid IVD, kit, nucleic acid technique (NAT)
   Sponsor: Roche Diagnostics Australia Pty Limited
   Manufacturer: Roche Molecular Systems Inc
2. **Atomo Diagnostics Pty Ltd - Atomo HIV self test -HIV1/ HIV2 antibody…**
   ARTG ID: 311989
   Product name: Atomo HIV self test - HIV1/HIV2 antibody IVD, kit, immunochromatographic test (ICT), rapid
   Sponsor: Atomo Diagnostics Pty Ltd
   Manufacturer: Atomo Diagnostics Pty Ltd
3. **Abbott Australasia Pty Ltd Diagnostic Division - Alinity s HIV Ag/Ab…**
   ARTG ID: 311748
   Product name: Alinity s HIV Ag/Ab Combo Assay - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
   Sponsor: Abbott Australasia Pty Ltd Diagnostic Division
   Manufacturer: Abbott GmbH & Co KG
4. **Roche Diagnostics Australia Pty Limited - PreciControl HIV;…**
   ARTG ID: 303171
   Product name: PreciControl HIV; HIV-2+GrpO - HIV1/HIV2 antigen/antibody IVD, control
   Sponsor: Roche Diagnostics Australia Pty Limited
   Manufacturer: Roche Diagnostics GmbH
5. **Roche Diagnostics Australia Pty Limited - PreciControl HIV Gen II -…**
   ARTG ID: 303170
   Product name: PreciControl HIV Gen II - HIV1/HIV2 antigen/ antibody IVD, control
   Sponsor: Roche Diagnostics Australia Pty Limited
   Manufacturer: Roche Diagnostics GmbH
6. **Roche Diagnostics Australia Pty Limited - Elecsys HIV Duo - HIV1/HIV2 …**
   ARTG ID: 303169
   Product name: Elecsys HIV Duo - HIV1/HIV2 antigen/ antibody IVD, kit, chemiluminescent immunoassay
   Sponsor: Roche Diagnostics Australia Pty Limited
   Manufacturer: Roche Diagnostics GmbH
7. **Abbott Australasia Pty Ltd Diagnostic Division - Alinity i HIV Ag/Ab…**
   ARTG ID: 299664
   Product name: Alinity i HIV Ag/Ab Combo - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
   Sponsor: Abbott Australasia Pty Ltd Diagnostic Division
   Manufacturer: Abbott GmbH & Co KG
8. **Ortho-Clinical Diagnostics Australia Pty Ltd - VITROS…**
   ARTG ID: 299339
   Product name: VITROS Immunodiagnostic Products HIV Combo - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
   Sponsor: Ortho-Clinical Diagnostics Australia Pty Ltd
   Manufacturer: Ortho-Clinical Diagnostics
9. **Roche Diagnostics Australia Pty Limited - cobas HIV-1 for use on the…**
   ARTG ID: 294066
   Product name: cobas HIV-1 for use on the cobas 6800/8800 Systems - HIV1 nucleic acid IVD, kit, nucleic acid technique (NAT)
   Sponsor: Roche Diagnostics Australia Pty Limited
   Manufacturer: Roche Diagnostics GmbH
10. **Roche Diagnostics Australia Pty Limited - cobas HBV/HCV/ HIV-1 Control…**
    ARTG ID: 294020
    Product name: cobas HBV/HCV/HIV-1 Control Kit for use on the cobas 4800 System - HIV1/Hepatitis C virus/Hepatitis B virus nucleic acid IVD, control
    Sponsor: Roche Diagnostics Australia Pty Limited
    Manufacturer: Roche Diagnostics GmbH
11. **Roche Diagnostics Australia Pty Limited - cobas HIV-1 for use on the…**
    ARTG ID: 294019
    Product name: cobas HIV-1 for use on the cobas 4800 System - HIV1 nucleic acid IVD, kit, nucleic acid technique (NAT)
    Sponsor: Roche Diagnostics Australia Pty Limited
    Manufacturer: Roche Diagnostics GmbH
12. **Roche Diagnostics Australia Pty Limited - cobas HBV/HCV/ HIV-1 Control…**
    ARTG ID: 294018
    Product name: cobas HBV/HCV/HIV-1 Control Kit for use on the cobas 6800/8800 Systems - HIV1/Hepatitis C virus/ Hepatitis B virus nucleic acid IVD, control
    Sponsor: Roche Diagnostics Australia Pty Limited
    Manufacturer: Roche Diagnostics GmbH
13. **Vela Diagnostics Australia Pty Ltd - Human immunodeficiency virus…**
    ARTG ID: 291546
    Product name: Human immunodeficiency virus (HIV) IVDs
    Sponsor: Vela Diagnostics Australia Pty Ltd
    Manufacturer: Vela Operations Singapore Pte Ltd
14. **Bio-Rad Laboratories Pty Ltd - Access HIV Combo QC4 & QC5 -…**
    ARTG ID: 289821
    Product name: Access HIV Combo QC4 & QC5 - HIV1/HIV2 antigen/antibody IVD, control
    Sponsor: Bio-Rad Laboratories Pty Ltd
    Manufacturer: Bio-Rad

15. **Abbott Australasia Pty Ltd Molecular Division - Human…**
ARTG ID: 286713
Product name: Human immunodeficiency virus (HIV) IVDs
Sponsor: Abbott Australasia Pty Ltd Molecular Division
Manufacturer: Abbott Molecular Inc

16. **DiaSorin Australia Pty Ltd - LIAISON XL MUREX HIV Ab/Ag HT -…**
ARTG ID: 279803
Product name: LIAISON XL MUREX HIV Ab/Ag HT - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: DiaSorin Australia Pty Ltd
Manufacturer: DiaSorin SpA

17. **Inverness Medical Innovations Australia Pty Ltd T/A Alere - Alere HIV …**
ARTG ID: 276049
Product name: Alere HIV Combo - HIV1/HIV2 antigen/antibody IVD, kit, immunochromatographic test (ICT), rapid
Sponsor: Inverness Medical Innovations Australia Pty Ltd T/A Alere
Manufacturer: Alere Medical Co Ltd

18. **Hologic Australia Pty Ltd - Aptima HIV-1 Quant Dx Calibrator Kit,…**
ARTG ID: 269682
Product name: Aptima HIV-1 Quant Dx Calibrator Kit, PRD-03001 - HIV1 nucleic acid IVD, calibrator
Sponsor: Hologic Australia Pty Ltd
Manufacturer: Hologic Inc

19. **Hologic Australia Pty Ltd - Aptima HIV-1 Quant Dx Controls Kit,…**
ARTG ID: 269681
Product name: Aptima HIV-1 Quant Dx Controls Kit, PRD-03002 - HIV1 nucleic acid IVD, control
Sponsor: Hologic Australia Pty Ltd
Manufacturer: Hologic Inc

20. **Hologic Australia Pty Ltd - Aptima HIV-1 Quant DX Assay Kit,…**
ARTG ID: 269680
Product name: Aptima HIV-1 Quant DX Assay Kit, PRD-03000 - HIV1 nucleic acid IVD, kit, nucleic acid technique (NAT)
Sponsor: Hologic Australia Pty Ltd
Manufacturer: Hologic Inc

21. **DiaSorin Australia Pty Ltd - Murex HIV-1.2.O - HIV1/HIV2 antibody…**
ARTG ID: 264533
Product name: Murex HIV-1.2.O - HIV1/HIV2 antibody IVD, kit, enzyme immunoassay (EIA)
Sponsor: DiaSorin Australia Pty Ltd
Manufacturer: DiaSorin Spa UK Branch

22. **Cepheid Holdings Pty Ltd - Human immunodeficiency virus (HIV) IVDs**
ARTG ID: 259967
Product name: Human immunodeficiency virus (HIV) IVDs
Sponsor: Cepheid Holdings Pty Ltd
Manufacturer: Cepheid AB

23. **Abbott Australasia Pty Ltd Molecular Division - Human…**
ARTG ID: 258054
Product name: Human immunodeficiency virus (HIV) IVDs
Sponsor: Abbott Australasia Pty Ltd Molecular Division
Manufacturer: Celera Corporation

24. **Ortho-Clinical Diagnostics Australia Pty Ltd - VITROS Anti-HIV 1 + 2…**
ARTG ID: 251957
Product name: VITROS Anti-HIV 1 + 2 - HIV1/HIV2 antibody IVD, kit, chemiluminescent immunoassay\
Sponsor: Ortho-Clinical Diagnostics Australia Pty Ltd
Manufacturer: Ortho-Clinical Diagnostics

25. **Immuno Pty Ltd - Uni-Gold HIV - HIV1/HIV2 antibody IVD, kit,…**
ARTG ID: 240814
Product name: Uni-Gold HIV - HIV1/HIV2 antibody IVD, kit, immunochromatographic test (ICT), rapid
Sponsor: Immuno Pty Ltd
Manufacturer: Trinity Biotech Plc

26. **Integrated Sciences Pty Ltd - OraQuick ADVANCE® Rapid HIV-1/2…**
ARTG ID: 240813
Product name: OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test and Kit Controls - HIV1/HIV2 antibody IVD, kit, immunochromatographic test (ICT), rapid
Sponsor: Integrated Sciences Pty Ltd
Manufacturer: Orasure Technologies Inc

27. **Siemens Healthcare Pty Ltd - ADVIA Centaur HIV 1/O/2 Enhanced (EHIV)…**
ARTG ID: 239117
Product name: ADVIA Centaur HIV 1/O/2 Enhanced (EHIV) - HIV1/HIV2 antibody IVD, kit, chemiluminescent immunoassay
Sponsor: Siemens Healthcare Pty Ltd
Manufacturer: Siemens Healthcare Diagnostics Inc

28. **Bio-Rad Laboratories Pty Ltd - Access HIV Combo QC - HIV1/HIV2…**
ARTG ID: 237303
Product name: Access HIV Combo QC - HIV1/HIV2 antigen/antibody IVD, control
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

29. **Bio-Rad Laboratories Pty Ltd - Access HIV Combo Calibrators -…**
ARTG ID: 237302
Product name: Access HIV Combo Calibrators - HIV1/HIV2 antigen/antibody IVD, calibrator
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

30. **Biomerieux Australia Pty Ltd - bioMerieux SA VIDAS HIV DUO Ultra -…**
ARTG ID: 233218
Product name: bioMerieux SA VIDAS HIV DUO Ultra - HIV1/HIV2 antigen/antibody IVD, kit, enzyme immunoassay (EIA)
Sponsor: Biomerieux Australia Pty Ltd
Manufacturer: Biomerieux SA

31. **Inverness Medical Innovations Australia Pty Ltd T/A Alere - Determine…**
ARTG ID: 232594
Product name: Determine HIV-1/2 - HIV1/HIV2 antibody IVD, kit, immunochromatographic test (ICT), rapid
Sponsor: Inverness Medical Innovations Australia Pty Ltd T/A Alere
Manufacturer: Alere Medical Co Ltd

32. **Bio-Rad Laboratories Pty Ltd - Geenius™ HIV 1/2 Confirmatory Controls…**
ARTG ID: 229652
Product name: Geenius™ HIV 1/2 Confirmatory Controls - HIV1/HIV2 antibody IVD, control
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

33. **Bio-Rad Laboratories Pty Ltd - Geenius™ HIV 1/2 Confirmatory Assay -…**
ARTG ID: 229064
Product name: Geenius™ HIV 1/2 Confirmatory Assay - HIV1/HIV2 antibody IVD, kit, immunochromatographic test (ICT), rapid
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

34. **Roche Diagnostics Australia Pty Limited - PreciControl HIV 1, 2, 3 -…**
ARTG ID: 226161
Product name: PreciControl HIV 1, 2, 3 - HIV1 antigen/antibody IVD, control
Sponsor: Roche Diagnostics Australia Pty Limited
Manufacturer: Roche Diagnostics GmbH

35. **Roche Diagnostics Australia Pty Limited - Elecsys HIV Combi PT -…**
ARTG ID: 226069
Product name: Elecsys HIV combi PT (Modular Analytics E170, cobas e 411/601/602) - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: Roche Diagnostics Australia Pty Limited
Manufacturer: Roche Diagnostics GmbH

36. **Bio-Rad Laboratories Pty Ltd - Genscreen ULTRA HIV Ag-Ab - HIV1/HIV2…**
ARTG ID: 220632
Product name: Genscreen ULTRA HIV Ag-Ab - HIV1/HIV2 antigen/antibody IVD, kit, enzyme immunoassay (EIA)
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

37. **Bio-Rad Laboratories Pty Ltd - Genscreen HIV-1 Ag Confirmatory Assay…**
ARTG ID: 220068
Product name: Genscreen HIV-1 Ag Confirmatory Assay - HIV1 antigen neutralization IVD, kit, enzyme immunoassay (EIA)
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

38. **Bio-Rad Laboratories Pty Ltd - Genscreen HIV-1 Antigen Assay - HIV…**
ARTG ID: 220067
Product name: Genscreen HIV-1 Antigen Assay - HIV1 antigen IVD, kit, enzyme immunoassay (EIA)
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

39. **Bio-Rad Laboratories Pty Ltd - Genscreen™ HIV-1/2 Version 2 -…**
ARTG ID: 220061
Product name: Genscreen™ HIV-1/2 Version 2 - HIV1/HIV2 antibody IVD, kit, enzyme immunoassay (EIA)
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

40. **Abbott Australasia Pty Ltd Molecular Division - Human…**
ARTG ID: 217841
Product name: Human immunodeficiency virus (HIV) IVDs
Sponsor: Abbott Australasia Pty Ltd Molecular Division
Manufacturer: Abbott Molecular Inc

41. **Abbott Australasia Pty Ltd Diagnostic Division - ARCHITECT HIV Ag/Ab…**
ARTG ID: 213306
Product name: ARCHITECT HIV Ag/Ab Combo assay - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: Abbott Australasia Pty Ltd Diagnostic Division
Manufacturer: Abbott GmbH & Co KG

42. **Abbott Australasia Pty Ltd Diagnostic Division - PRISM HIV Ag/Ab…**
ARTG ID: 212528
Product name: PRISM HIV Ag/Ab combo assay - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: Abbott Australasia Pty Ltd Diagnostic Division
Manufacturer: Abbott GmbH & Co KG

43. **MP Biomedicals Australasia Pty Ltd - MP Diagnostics HIV Blot 2.2…**
ARTG ID: 212462
Product name: MP Diagnostics HIV Blot 2.2 assay - HIV1/HIV2 antibody IVD, kit, immunoblot
Sponsor: MP Biomedicals Australasia Pty Ltd
Manufacturer: MP Biomedicals Asia Pacific Pte Ltd

44. **DiaSorin Australia Pty Ltd - LIAISON XL MUREX HIV Ab / Ag - HIV1/HIV2…**
ARTG ID: 212434
Product name: LIAISON XL MUREX HIV Ab / Ag - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: DiaSorin Australia Pty Ltd
Manufacturer: DiaSorin SpA

45. **Qiagen Pty Ltd - Human immunodeficiency virus (HIV) IVDs**
ARTG ID: 210376
Product name: Human immunodeficiency virus (HIV) IVDs
Sponsor: Qiagen Pty Ltd
Manufacturer: Qiagen GmbH

46. **Bio-Rad Laboratories Pty Ltd - Access HIV Combo - HIV1/HIV2...**
ARTG ID: 207994
Product name: Access HIV Combo - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: Bio-Rad Laboratories Pty Ltd
Manufacturer: Bio-Rad

47. **Siemens Healthcare Pty Ltd - ADVIA Centaur HIV Ag/Ab Combo (CHIV) -...**
ARTG ID: 205090
Product name: ADVIA Centaur HIV Ag/Ab Combo (CHIV) - HIV1/HIV2 antigen/antibody IVD, kit, chemiluminescent immunoassay
Sponsor: Siemens Healthcare Pty Ltd
Manufacturer: Siemens Healthcare Diagnostics Inc

48. **Siemens Healthcare Pty Ltd - Human immunodeficiency virus (HIV) IVDs**
ARTG ID: 185755
Product name: Human immunodeficiency virus (HIV) IVDs
Sponsor: Siemens Healthcare Pty Ltd
Manufacturer: Siemens Healthcare Diagnostics Inc

49. **Roche Diagnostics Australia Pty Limited - Human immunodeficiency...**
ARTG ID: 180220
Product name: Human immunodeficiency virus (HIV) IVDs - Human immunodeficiency virus (HIV) IVDs
Sponsor: Roche Diagnostics Australia Pty Limited
Manufacturer: Roche Molecular Systems Inc

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