

Prescribing pre-exposure prophylaxis for HIV

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[HIV diagnoses in Australia fall as clinicians embrace pre-exposure prophylaxis](#)

SUMMARY

Co-formulated tenofovir disoproxil plus emtricitabine is highly effective as pre-exposure prophylaxis for HIV.

It is suitable for men who have sex with men, for heterosexual sex and for people who use intravenous drugs when there is a risk of HIV infection.

Pre-exposure prophylaxis is one pill per day and can be prescribed by all medical practitioners and nurse practitioners via the Pharmaceutical Benefits Scheme. It is best prescribed in a three-monthly program with regular monitoring for patient adherence, safety, HIV and other sexually transmitted infections.

Prophylaxis is well tolerated but requires monitoring for kidney toxicity and low bone density.

Introduction

In addition to preventing new HIV infection in individuals, and the fears associated with this, pre-exposure prophylaxis (PrEP) has been a major public health development for the community.

HIV is no longer a terminal diagnosis, but can be well managed as a chronic condition with almost normal life expectancy. Nevertheless, there is a burden of comorbidities associated with HIV infection due to increased inflammation even with virus suppression. There are also the lifelong costs of treatment.

With variable use of condoms and in the absence of an HIV vaccine, other measures have been necessary to reduce HIV transmission. Since 2000, there was a gradual increase in new HIV diagnoses in Australia, particularly in men who have sex with men. Since 2012, state health authorities have attempted to tackle the rising incidence more systematically. Initial approaches included increased testing to identify undiagnosed cases, and encouraging treatment of every person with HIV to reduce viral load and transmission in the community (known as treatment as prevention or TasP). This resulted in a plateauing but not a reduction of new diagnoses. Only since the widespread uptake of PrEP in 2016¹ has there been a dramatic fall in new infections (see editorial in this issue). There has been a reduction of up to 50% in men who have sex with men living in inner cities.¹

Drugs used for prophylaxis

Currently licensed PrEP in Australia consists of co-formulated tenofovir disoproxil 300 mg plus emtricitabine 200 mg. One pill is taken daily, ideally with food which increases drug concentrations by up to 40%. Both compounds inhibit nucleoside reverse transcriptase. This is an essential step for the virus in

which single-stranded RNA is converted to double-stranded RNA so the virus can enter the host cell nucleus, integrate, and then replicate.

The intracellular half-lives of tenofovir disoproxil and emtricitabine are long – 150 hours and 39 hours. This enables some leniency in terms of dosing and adherence for men who have sex with men taking PrEP.

The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) updated their [PrEP Guidelines](#), which provide comprehensive guidance for prescribing PrEP in the Australian context.

Who is suitable for PrEP?

PrEP is indicated for people who are at risk of HIV infection, or have fears related to acquiring it. Men who have sex with men account for approximately 70% of HIV diagnoses in Australia. A high risk of HIV infection has been associated with:

- unprotected receptive anal intercourse
- a history of sexually transmitted infections, particularly anorectal gonorrhoea and chlamydia
- use of illicit drugs, particularly crystal methamphetamine because of its effect on behaviour.

Sex workers and people who use intravenous drugs are also at risk of HIV, as are some transgender people and heterosexuals who engage in high-risk behaviour.

While PrEP has been particularly effective in reducing new HIV infections in Australian-born men who have sex with men, there is a need to ensure the provision of PrEP to overseas-born men who have sex with men, heterosexuals at risk, and Aboriginals. These groups have not shown declines in new HIV infections.

PrEP is not recommended in people who already have HIV because dual therapy with tenofovir disoproxil/emtricitabine is insufficient to suppress HIV and there is a risk of drug resistance developing. Additional drugs are needed for HIV treatment regimens.

How to prescribe PrEP

PrEP is available on the Pharmaceutical Benefits Scheme (PBS) via streamlined S85 monthly prescription. Any medical practitioner or qualified nurse practitioner can prescribe up to three months supply. For those who are ineligible through Medicare, the options are via private prescription, or patient importation via online pharmacies (a prescription is required for Customs). [PrEPaccessNow](#) is a useful link for reliable online pharmacy sites.

The most effective way to prescribe tenofovir disoproxil/emtricitabine is in a PrEP program. This recommends three-monthly follow-up visits for clinical and laboratory assessment and prescribing of PrEP (see Table). Visits involve regular monitoring for adherence, potential adverse reactions and, with the patient's agreement, for sexually transmitted infections and HIV infection.

At the initial visit, patients should be advised that while PrEP is highly effective in preventing HIV infection, it does not protect against other sexually transmitted infections and condom use is encouraged.

PrEP is not recommended if the estimated glomerular filtration rate (eGFR) is less than 60 mL/min/1.73 m² so kidney function should be

Table Laboratory evaluation and clinical follow-up of individuals who are prescribed pre-exposure prophylaxis

Test	Baseline (week 0)	1 month after starting PrEP (optional but recommended in some jurisdictions)	3 months after starting PrEP	Every subsequent 3 months on PrEP	Other frequency
HIV testing and assessment for signs or symptoms of acute infection	Y	Y	Y	Y	N
Assess adverse 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 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	Y	N	Y	N	At least every 6 months or according to risk of chronic kidney disease
Urine protein:creatinine ratio	Y	N	Y	N	Every 6 months
Pregnancy test (for women of child-bearing age)	Y	Y	Y	Y	N

Y Yes
 N No
 MSM Men who have sex with men
 STI sexually transmissible infection
 eGFR estimated glomerular filtration rate
 Source: [ASHM PrEP Guidelines September 2019 update](#)

measured at baseline. Patients with an eGFR below 60 mL/min/1.73 m² should be referred to a specialist for management. Other potential issues such as low bone density should also be assessed. The use of concomitant drugs that could potentiate toxicity such as non-steroidal anti-inflammatory drugs should be avoided, as well as pre-existing HIV infection (by fourth generation HIV antibody/antigen blood testing) and other sexually transmitted infections.

Some practitioners may elect to review the patient after one month to assess any issues related to PrEP adherence, toxicity, and re-test for HIV infection.

How effective is PrEP?

PrEP taken daily reduces HIV infection via sexual transmission by 99%.² Lower adherence reduces PrEP effectiveness – if four pills are taken per week, effectiveness is reduced to 96% and falls rapidly after that as adherence drops. Transmission via intravenous drug use was reduced by 74% in those with detectable tenofovir levels.³

Tenofovir disoproxil/emtricitabine is highly effective as PrEP because high drug concentrations are rapidly achieved in rectal tissue. This is less so in vaginal tissue and to maintain optimal drug concentrations in women, daily adherence should be emphasised. Steady state drug concentrations of tenofovir disoproxil are achieved in genital and rectal tissues by one week, and in blood by 20 days.

For men who have sex with men, a loading dose of two pills with subsequent daily dosing will enable effectiveness of PrEP from two hours after first administration. For men and women practising at-risk heterosexual sex and for those who are transgender, PrEP is effective after seven days of daily dosing.

Adherence

Illicit drug use may affect adherence to PrEP, and drug and alcohol issues may need to be addressed. Adherence can be supported with increased knowledge about PrEP and its effectiveness as well as dealing with adverse effects and concerns about toxicity.

Patients may take PrEP for periods of time at risk and then stop if they enter into a monogamous relationship. For men who have sex with men, stopping PrEP is safe after they have taken a 24- and 48-hour dose following the last sexual exposure. For men and women engaging in heterosexual sex and people who use intravenous drugs, it is recommended to continue PrEP for 28 days after their last exposure.

Adolescents and young adults taking PrEP are more likely to discontinue PrEP so may require more frequent monitoring to support adherence.

Adverse effects, drug interactions and monitoring

It is rare for PrEP to be stopped because of adverse events. Initial adverse effects tend to be transient and include gastrointestinal (e.g. nausea and diarrhoea) and central nervous system events (e.g. headache lasting a week or slightly longer).

Kidney and liver toxicity are rare but regular monitoring is required. Patients aged over 40 years with eGFR less than 90 mL/min/1.73 m², hypertension or diabetes or taking concomitant nephrotoxic drugs should have three-monthly renal assessment (see Table).

Tenofovir disoproxil and emtricitabine are renally excreted via glomerular filtration and tubular secretion. There are potential drug–drug interactions that can adversely affect renal function. These can occur with concomitant use of renally excreted drugs such as non-steroidal anti-inflammatory drugs, aminoglycosides, aciclovir and valaciclovir. Characteristically, renal complications involve proximal tubular damage, leading to acute kidney injury, Fanconi syndrome or chronic kidney disease. There can also be a milder ‘creatinine creep’ with gradually increasing creatinine and decreasing eGFR over time.

Tenofovir disoproxil is associated with reduced bone density of 3–4% in the first year of treatment. This plateaus out to normal bone density loss of 1% per year (after the age of 30 years). For the majority of PrEP users, this bone density reduction is not clinically significant. However, for those over 40 years of age who are at risk of low bone density, bone density can be assessed using the FRAX fracture risk assessment score, or dual-energy X-ray absorptiometry (DXA) scanning. This is Medicare reimbursable under certain criteria, as outlined in [Osteoporosis Australia's bone density testing brochure for general practice](#).

PrEP can be used in patients with hepatitis B infection. However, interrupting PrEP can lead to a symptomatic flare of hepatitis B or drug resistance so these patients should be monitored closely.

On-demand PrEP

On-demand or intermittent use of PrEP has demonstrated effectiveness for men who have sex with men.⁴ Two pills of tenofovir disoproxil/emtricitabine are taken 2–24 hours before sex, followed by a single pill 24 hours and 48 hours after the initial dose. If there is further sexual activity, PrEP can continue to be taken daily for two subsequent days following the last sexual activity. On-demand PrEP is potentially suitable for those who have sexual contact on an occasional or intermittent basis and

are able to plan for these episodes. This method is endorsed in the ASHM guidelines as an alternative to daily PrEP for men who have sex with men, but is not recommended for those with hepatitis B infection, women, heterosexual men, and for those who are transgender.

Other PrEP medicines

The DISCOVER study demonstrated the effectiveness of tenofovir alafenamide co-formulated with emtricitabine as PrEP.⁵ This combination has reduced kidney and bone toxicity and is currently licensed in Australia only for HIV treatment.

There are currently studies of longer acting PrEP drugs such as injectable cabotegravir, an integrase strand transfer inhibitor given every second month, which has been found to be effective in treatment of HIV infection.⁶

Conclusion

PrEP provides a valuable, safe and effective method for medical practitioners to assist their patients in preventing HIV transmission. It can be prescribed in the community with regular monitoring every three months. <

Mark Bloch has participated on medical advisory boards for Gilead Sciences, VIV Healthcare and Abbvie. He has received support to attend scientific conferences from Gilead Sciences and has given lectures for Gilead Sciences, VIV Healthcare and Abbvie. His institution has received payments for clinical research from Gilead Sciences, VIV Healthcare, Abbvie, MSD, GSK, Eli-Lilly, Amgen and Pfizer.

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