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Update on HIV PrEP for HIV Clinicians

This communique is for clinicians involved in HIV, who may be consulted about HIV Pre-Exposure Prophylaxis (PrEP). It assumes an understanding of HIV prophylaxis.

Overview of the current status of PrEP in Australia:

There are currently three demonstration projects in Australia looking at the practicalities of introducing PrEP in the Australian setting. Truvada™, the drug used for PrEP, is listed on the Australian Register of Therapeutic Goods (ARTG) as a treatment for HIV infection, not as a prophylactic. An application for prophylactic use is likely to be lodged early in 2015. Daily use of Truvada™ has been registered for PrEP in the [USA](#), and is available via a number of mechanisms in other developed country settings internationally.

Consumers in Australia can currently access PrEP through a number of mechanisms: They can purchase the drug without subsidy; import drugs into Australia for private use under the [Personal Importation Scheme](#) (and we know that a number of people are using this option); or seek enrolment in one of the current projects in Australia.

ASHM recommends that any individual considering PrEP discuss this with a clinician experienced in HIV management. Although Truvada™ is not listed for PrEP it can be prescribed off-label. It is a pharmaceutical with potential side effects and care should be taken with its prescription. Consumers need to be aware that is being prescribed off-label; of the necessity to take the medication on a daily basis; the potential limitations if this dosing regimen is not maintained; and other preventative strategies to minimise the risk of exposure to HIV and other sexually transmissible (STI) and/or blood-borne infections. Furthermore, preliminary data from the Victorian PrEP Demonstration Project shows that at baseline 25 per cent of patients presenting for PrEP have an STI and one per cent are HIV seropositive. This highlights the need for clinical evaluation. Any patient who is on PrEP will need regular monitoring, prevention and adherence support, and will require maintenance prescriptions.

Evidence for the effectiveness of HIV PrEP:

Evidence has been growing in support of the efficacy of PrEP. The key feature in preventing transmission is establishing and maintaining a therapeutic, preventative serum level of drugⁱ. In late 2014, two trials stopped their placebo arms and offered all participants the active drug, given the differences which were observed between the active and control armsⁱⁱ, ⁱⁱⁱ. Both these studies will report in detail at CROI in late February 2015. While consumers and funders would like to know the least drug-heavy dose, adequate and simplified dosage is yet to be established and the optimum or minimum dosage and frequency is not yet determined. Long acting drugs which could be administered monthly or quarterly are being studied for both therapeutic and prophylactic applications.^{iv}



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Discussing PrEP with patients:

Some patients are well informed about developments in HIV medicine and will actively seek out prophylaxis. Other patients may not have heard of PrEP, or may not feel comfortable asking you about it. PrEP is a significant commitment and should be restricted to individuals who are at elevated risk of HIV acquisition: Men who have unprotected sex with multiple partners; people who share injecting equipment; and patients in a relationship with a person with HIV who is not on treatment or who does not have an undetectable viral load¹. Given the low prevalence of HIV in the community and the low but real risk of toxicity, daily PrEP should not be recommended for people at low risk. These patients should be counselled to use safer sex and safer injecting practices, but they should be encouraged to return to discuss PrEP if their situation changes and they become at high risk of acquiring HIV. Further guidance on how to establish a patient's level of HIV risk and eligibility for PrEP is provided in the [Australian PrEP Guidelines](#).

Establishing HIV status:

Whether people are presenting for post-exposure prophylaxis (PEP) or pre-exposure prophylaxis (PrEP), it is essential to establish their current HIV status. This should be done using a conventional blood sample and laboratory testing. If the result is negative this should be confirmed by a repeat test in two or more weeks if there has been recent exposure to HIV. Any individual, no matter how informed they are, may have HIV infection when they present for PEP or PrEP. Experience from presentations for PEP revealed that 1.5-2.0 per cent of people in Australia who thought they were negative actually had established HIV infection at the time they sought PEP. Failure to establish a correct baseline of HIV status would erroneously suggest that PrEP had failed to protect the individual².

In addition, if a person living with HIV fails to be diagnosed with HIV when they commence Truvada™ for PrEP or PEP there is a high likelihood that they will develop resistance to it as this medication alone is insufficient to treat HIV infection. This would then limit their future HIV treatment options.

Compliance with dosing regimen:

Current scientific evidence shows that when Truvada™ is used for PrEP, it needs to be taken daily to provide effective coverage. The IPREX study demonstrates a linear correlation between the concentration of Truvada™ in the blood and its preventative efficacy. In short: If you don't take it, it doesn't work! Truvada™ combines tenofovir and emtricitabine and it appears both drugs are necessary to provide effective protection³.

Condoms and safe injecting strategies:

Patients should be counselled to continue using condoms and safe injecting practices. This will provide additional protection from the transmission of HIV and also prevent the acquisition of other sexually transmissible and blood-borne infections.

¹ PrEP has been used in couples wanting to conceive for many years. If you have a patient or serodiscordant couple wanting to conceive you should refer to an HIV paediatric service.

² The IPREX study had one seroconversion. This individual had established infection at the first review, suggesting that he had been exposed at enrolment.

³ Davies, O et. al. Failure of daily tenofovir to prevent HIV transmission or the establishment of a significant viral reservoir despite continued antiretroviral therapy. CROI 2014 Poster 199



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Monitoring and side effects:

ASHM strongly advises monitoring any patient initiated or managed on PrEP. There is a risk of side effects - particularly renal complications - with Truvada™ so regular monitoring of renal function is necessary. In addition, patients receiving nephrotoxic agents may not be eligible to commence Truvada™. It is also important to regularly test patients for HIV and other sexually transmissible and blood-borne infections. This will also provide an opportunity to discuss the continued need for PrEP. The [Australian Guidelines on the prescription of PrEP](#) guide the periodicity of clinical review and the online 2015 [ASHM HIV Management](#) contains detailed information about PrEP. Given that Truvada™ PrEP is being prescribed off-label, it is important that the prescriber understands their responsibilities and gains informed consent from the patient.

While PrEP is effective if taken at a therapeutic level, the importance of establishing and maintaining this cannot be over emphasised and individuals taking PrEP need to be fully apprised of this. Intermittent PrEP has the combined risk of facilitating HIV acquisition; removing tenofovir and emtricitabine from the treatment drugs available should HIV be acquired; and transmitting tenofovir and/or emtricitabine resistance. If a patient on Truvada™ PrEP does acquire HIV s/he will need to take additional drugs to treat HIV.

How long do my patients need to take PrEP?

PrEP should be used whilst the person remains at high risk of acquiring HIV infection. Current PrEP requires consistent usage, to establish an effective drug level to provide protection against the acquisition of HIV. IT IS NOT A MORNING AFTER PILL, NOR IS IT A ONE PILL BEFORE EXPOSURE PILL. Long-lasting injectable agents and possibly drug implants are being researched for their efficacy in preventing HIV infection^v, but they are not available yet.

Long-term implications and stopping PrEP:

We do not have a lot of experience in the long-term use of PrEP. It is expected that Truvada™ PrEP will be an option that people use for a period of time, and in the event that long-term injectable or slow release preparations are effective they will replace daily oral regimens. Ultimately, we hope that a vaccine will replace PrEP. In the interim, Truvada™ can provide an effective preventative.

The most likely negative sequelae of long-term PrEP are likely to be the development of resistance and, in a small number of people, the development of renal toxicity and loss of bone mineral density. If patients are not adherent to PrEP they should be counselled to stop taking it. Likewise, if renal toxicity cannot be managed PrEP should be stopped.

Accessing PrEP:

PrEP cannot be accessed through the PBS as Truvada™ is on the ARTG as an HIV treatment only. A separate application needs to be made by the manufacturer for use as PrEP. This has been done in the USA and the UK. It is anticipated that a TGA application will be made in the first quarter of 2015, but the current evaluation process would mean it would be at least 12 months before Truvada™ could be listed for PrEP. While that could make the drug available for prophylaxis purposes, a separate application would need to be made to the Pharmaceutical Benefits Advisory Committee (PBAC) to get subsidy through the PBS.



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Patients have a number of options to access PrEP. Truvada™ can be prescribed and purchased without subsidy at a cost in the vicinity of \$850 per bottle of 30 pills. Patients can also personally import the drug in person or via mail. Details of how to do this can be obtained on the [TGA website](#).

Generic drugs can be purchased via a number of websites. These drugs have not been evaluated by the TGA, but Truvada™ has been evaluated by the US regulator, the FDA. Generic tenofovir and emtricitabine (combined in a single tablet) will cost in the vicinity of \$130 per month or \$330 for a three month supply. Generic drugs use alternative trade names and packaging and may be a different colour or shape so you must be sure that the drug being purchased is the correct formulation. ACON has simple [step-by-step instructions](#) on their website on how to access PrEP using the personal importation scheme.

Self-importation has some risks associated with it. You do not have the quality protection provided by drugs evaluated and listed on the ARTG. You need to be careful about the veracity of the website. Supply time may vary and the postage time could be delayed if customs investigates the package. Self-importation is legal, but not routine. Having a valid Australian prescription, completed by a registered medical practitioner and completing all the paper work will facilitate the process but patients should allow up to eight weeks for delivery.

Contributing to PrEP studies:

The first PrEP study in Australia, VicPrEP, led by A/Prof Edwina Wright in Melbourne, is now full (for more information see www.vicprep.csrh.org). A large PrEP demonstration study, PRELUDE, led by Dr Iryna Zablotska from the Kirby Institute, is currently enrolling participants in NSW and is designed to provide access to PrEP to at least 300 people (for more information see <http://prelude.org.au/>). A smaller study led by A/Prof Darren Russell will commence recruitment in Queensland in April 2015 and information will be at www.hivfoundation.org.au once it becomes available.

How to order Generic Truvada™ for PrEP online:

The online supplier used for the purposes of this information sheet is *AIDS Drugs Online* <http://www.aids-drugs-online.com/> which sources low-cost generic versions of HIV medications from various overseas manufacturers. Other suppliers can be found by typing "aids drugs online" into your search engine. Please be aware that the brand names used on *AIDS Drugs Online* are not the same as the brands in Australia:

- a. Australian brand name: **Truvada**
- b. *AIDS Drugs Online* (ADO) brand name: **Tenvir EM**

Once you have obtained your prescription for Truvada™ (Tenvir EM) from your doctor, take the following steps to order Tenvir EM online.

1. Go to <https://www.aidsdrugsonline.net>
2. Type **Tenvir EM** into the **product search** area (in the orange box on the right side) and click on the **search** button.
3. Two options will then appear for selection (Tenvir EM 30 tabs @ \$104.98 & Tenvir EM 90 tabs @ \$313.36).
4. Select which option of Tenvir EM you would like to purchase.
5. As it can take some time for your order to reach Australia (up to eight weeks) it is worthwhile ordering at least a three month supply to avoid running out.



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6. Put your quantity (e.g. **1**) into the field next to **add to cart**. Then click **add to cart** button. An orange bar will appear at the top of the page showing what is in your cart.
7. Now click on the **Show Cart** button (in the orange bar). If this is your first time to ADO you will not have a username or password and this will be organised for you at this stage.
8. If you are happy with what is in your cart then scroll down to the bottom of the page to the payment section. You will be asked to **select a payment method** and most people will choose the **invoice me** option. Once you have chosen an option, select the **Check out now** button.
9. You will now be asked to fill out all your billing and personal information. Once this has been completed, select the **Register and Checkout** button on the top of the page. Please note some people may not want the medications to arrive at home and instead may use another address (consult with your doctor and pharmacist about the best address option. Some HIV clinics may agree to receive the drugs for you).
10. Once you complete the checkout process, you will receive a receipt for your order. You will also need to print the **patient release form** and sign it, indicating that you accept.
11. Once this is complete you can either:
 - a. **Scan/Email** your prescription and release form by replying to the receipt that you receive for your order. Or send these to admin@aidsdrugsnet.net quoting your order number in the subject line.
 - b. **Fax to this USA number:** 1-866-795-9461

ⁱ IPREX LB31 Conference on Retroviruses and Opportunistic Infections 2012. 76% efficacy at twice weekly, 96% efficacy at thrice weekly and 99% at daily dosing

ⁱⁱ <http://ashm.info/test-and-treat/arv-based-prevention> PROUD will be presenting at CROI 2015, it closed its control arm due to inferior performance

ⁱⁱⁱ <http://ashm.info/test-and-treat/arv-based-prevention> IPERGAY will be presenting at CROI 2015, it closed its control arm due to inferior performance

^{iv} Spreen, W.R., Margolis, D.A. & Pottage, J.C. Jr Long-acting injectable antiretrovirals for HIV treatment and prevention. *Curr Opin HIV AIDS*. 2013 Nov, 8(6): 565-71

^v Cooper, D.A. (2014), Where are we headed with ART? Beyond an undetectable viral load. FRPL01 AIDS2014 Melbourne.

Helpful links:

TGA Personal Importation Scheme <https://www.tga.gov.au/personal-importation-scheme>

ACON Ending HIV and PrEP Access <http://endinghiv.org.au/nsw/stay-safe/prep/>

ASHM PrEP Guidelines <http://arv.ashm.org.au/arv-guidelines/prep-resources-for-clinicians>

ASHM ARV Guidelines commentary <http://arv.ashm.org.au/>

ASHM HIV Management Biomedical Prevention Chapter

FDA PrEP Consumer info <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm311821.htm>

FDA PrEP announcement, approval of Truvada

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm312210.htm>

NSW PrEP study <http://prelude.org.au/>

Queensland PrEP study and PrEP Information www.hivfoundation.org.au

Victorian PrEP Study www.vicprep.csrh.org

For further information:

Visit the ASHM website www.ashm.org.au the ACON <http://endinghiv.org.au> Queensland HIV Foundation www.hivfoundation.org.au or contact the ASHM office during office hours 02 82040700