NZSHS
THE NEW ZEALAND SEXUAL HEALTH SOCIETY
SEXUAL HEALTH FOR ALL

20 November 2015

Funding Applications
Pharmac
POBox 10-254
Wellington 6143

Dear Pharmac,

Application: **Expanded access to HIV antiretroviral therapy for all individuals with confirmed HIV infection**

Applicants:
New Zealand Sexual Health Society
ADHB Auckland City Hospital Adult Infectious Disease Outpatient Clinic
ADHB Auckland Sexual Health Service, Greenlane Clinical Centre
BOPDHB Infectious Diseases & Sexual Health Physicians
CCDHB Infectious Diseases Department
CDHB Department of Infectious Diseases
New Zealand AIDS Foundation
Body Positive
Positive Women Inc
INA (Maori, Indigenous & South Pacific) HIV / AIDS Foundation
Te Whāriki Takapou
Gay Men's Sexual Health research group, University of Auckland
AIDS Epidemiology Group, University of Otago

We urgently ask Pharmac to reconsider eligibility for initiating HIV antiretroviral therapy (ART):

- Currently eligibility for commencing ART is limited to individuals with confirmed HIV infection and a CD4+ count of 500 cells/mm3 or under or who are symptomatic.

- In February 2014 Pharmac received advice from the PTAC Anti-Infective Subcommittee recommending all HIV positive individuals be eligible for ART. This recommendation came with a medium priority.[1]

- Since then a number of significant developments have occurred that we believe justify a reconsideration.

- *We strongly request Pharmac to make ART available without restriction to all asymptomatic individuals with confirmed HIV infection regardless of CD4+ count.*

Our application is based on the following developments:

1. START and TEMPRANO randomised clinical trial findings

In July 2015 evidence from the Strategic Timing of AntiRetroviral Treatment (START) randomised clinical trial was published in the *New England Journal of Medicine.*[2] The study was conducted at 215 sites in 35 countries and enrolled 4685 HIV-infected ART-naïve men and women with initial CD4+ counts above 500 cells/mm3. Approximately half were randomised to initiate ART immediately (early treatment) and half were randomised to defer ART until their CD4+ count declined to 350 cells/mm3 (deferred treatment). The study measured a combination of outcomes that included: (1) serious AIDS events (such as AIDS-related cancer), (2) serious non-AIDS events (major cardiovascular, renal and liver disease and cancer), and (3) death.

- *The interim analysis found the risk of developing serious illness or death was 57% lower among those in the early treatment group, compared to those in the deferred group.*

The TEMPRANO ANRS Study was also published in July 2015.[3] This followed 2056 patients in Ivory Coast randomised to one of four treatment groups.

- *This found that early ART initiation at CD4+ >500 was associated with a 44% lower risk of death or severe HIV-related illness than deferral of ART.*

An accompanying editorial noted that these large trials showed a minimal or no overall increase in adverse events in patients initiating ART early.[4]

2. World Health Organization and regional professional bodies revised ART guidelines

On 30 September 2015 the World Health Organization (WHO) revised their international guidelines on HIV treatment initiation.[5] The new recommendations are based on evidence from clinical trials and observational studies since 2013 indicating that earlier use of ART results in better clinical outcomes for people living with HIV compared to deferred treatment.

- *WHO now advises that ART should be initiated in everyone living with HIV at any CD4 count.*

Regional professional bodies have also amended their recommendations, including:

United States Department of Health and Human Services (USDHHS) [6]
Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) [7]
British HIV Association (BHIVA) [8]
European AIDS Clinical Society (EACS) [9]

- *Major professional bodies now recommend ART for all HIV infected adults living with HIV regardless of CD4 count.*

3. Prevention benefits of ART

The final results of the HPTN 052 study on HIV transmission were presented in July 2015. In this cohort of HIV discordant mostly heterosexual couples, ART conferred a 93% protective effect.[10] Interim analyses of two further cohort studies presented in 2014 [11] and 2015 [12] found no HIV transmissions between HIV serodiscordant gay and bisexual male couples where the HIV infected partner had an undetectable viral load. Although a very low rate of transmission cannot be ruled out, the evidence strongly indicates that ART offers a high degree of protection between individuals under ideal circumstances.

Subsequently the public health impact of offering ART to newly infected individuals has been modelled in Australia. In a paper presented in September 2015, Gray et al.[13] estimated that 10.3% of Australia's HIV infected population in 2014 were undiagnosed, 15.1% were diagnosed but not on ART, 8.2% were diagnosed, receiving ART with a detectable viral load, and 66.3% were diagnosed, on ART with an undetectable viral load. The researchers then estimated the contribution of each group to new HIV infections, being 44.9%, 38.4%, 5.5% and 11.1% respectively. Providing ART to individuals with diagnosed HIV but not currently on ART is therefore a public health priority for HIV prevention. The money invested in offering early ART would reduce the costs associated with treating more HIV cases.

- *The relatively small group of HIV infected individuals diagnosed but not on ART contributes disproportionately to new HIV infections as their virus is not suppressed.*

4. Nominal cost of extending ART in New Zealand

The cost of extending ART eligibility in the New Zealand context will be nominal. The Adult Infectious Disease Outpatient Clinic at Auckland City Hospital cares for approximately 50% of New Zealand's population with diagnosed HIV infection. Of these, as of October 2014 an estimated 90.5% are currently on ART, 5% (44 individuals) have CD4+ counts of >500 and are not on ART, and 4.5% are eligible but have chosen not to start or to continue with medication (Dr Simon Briggs pers comm 17 November 2015). This suggests that a mere 100 individuals New Zealand-wide would be newly eligible should the criteria change.

- *The cost of extending ART eligibility will affect approximately 5% of all individuals with diagnosed HIV infection, or only around 100 individuals across New Zealand.*

Furthermore, declining drug costs mean expanded access is not likely to increase overall expenditure on ART. For example, the price of subsidised efavirenz has fallen from $5700 to $761 per annum.

5. ART eligibility key to incentivising HIV testing and early diagnosis

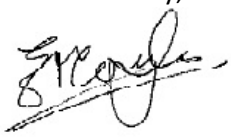
There is now unambiguous evidence that a timely diagnosis of HIV infection and early treatment maximises personal wellbeing and minimises onward transmission. Community organisations have consequently increased promotion of HIV testing of those most at risk, in 2015 initiating "HIV Testing Month". If ART were available immediately to all those newly diagnosed it would provide a strong additional incentive for those considering an HIV test.

- *Currently not all those newly diagnosed are able to access HIV treatment, potentially delaying the choice to test for HIV among those with undiagnosed infection who are the most implicated in onward transmission.*

In summary, universal access to ART is the most important clinical priority for the treatment of HIV infection. Universal ART will not be expensive in the New Zealand context. Early access to ART is also likely to become cost-saving due to the secondary HIV transmissions averted.

Thank you for considering this application and we would be happy to provide more information.

Yours sincerely,



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Supporting applicants (representative):
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BOPDHB Infectious Diseases & Sexual Health Physicians (c/o Dr Massimo Giola)
CCDHB Infectious Diseases Department (c/o Dr Nigel Raymond)
CDHB Department of Infectious Diseases (c/o Dr Sarah Metcalf)
New Zealand AIDS Foundation (c/o Shaun Robinson)
Body Positive (c/o Mark Fisher)
Positive Women Inc (c/o Jane Bruning)
INA (Maori, Indigenous & South Pacific) HIV/AIDS Foundation (c/o Marama Pala)
Te Whāriki Takapou (c/o Alison Green)
Gay Men's Sexual Health research group, University of Auckland (c/o Dr Peter Saxton)
AIDS Epidemiology Group, University of Otago (c/o A/Prof Nigel Dickson)

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[1] PTAC Anti-Infective Subcommittee meeting held 26 February 2014 minutes for web publishing. Available online at: https://www.pharmac.health.nz/assets/ptac-anti-infective-subcommittee-minutes-2014-02.pdf
[2] The INSIGHT START Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. N Engl J Med. 2015; 373:795-807. **[attached]**
[3] The TEMPRANO ANRS 12136 Study Group. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. N Engl J Med. 2015; 373:808-22. **[attached]**
[4] Abdool Karim SS. Overcoming Impediments to Global Implementation of Early Antiretroviral Therapy. N Engl J Med. 2015; 373:875-876. **[attached]**
[5] WHO. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. 2015. Available online at: http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/
[6] US Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. 2015. Available online at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/10/initiating-art-in-treatment-naive-patients
[7] ASHM. Antiretroviral Guidelines: US DHHS Guideline with Australian commentary – When to start antiretroviral therapy in people with HIV. 2015. Available online at: http://arv.ashm.org.au/clinical-guidance
[8] British HIV Association. BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015. Available online at: http://www.bhiva.org/HIV-1-treatment-guidelines.aspx
[9] European AIDS Clinical Society. Guidelines version 8.0 October 2015. Available online at: http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html
[10] Cohen M et al. Final results of the HPTN 052 randomized controlled trial: antiretroviral therapy prevents HIV transmission. J Int AIDS Soc. 2015;18(5Suppl. 4): 20479. **[attached]**
[11] Rodger A et al. HIV transmission risk through condomless sex if HIV+ partner on suppressive ART: PARTNER Study. 21st CROI, 3-6 March 2014, Boston. Oral late breaker abstract 153LB.
[12] Grulich AE et al on behalf of the Opposites Attract Study Group. HIV Transmission in Male Serodiscordant Couples in Australia, Thailand and Brazil. Presented at CROI, Seattle, 2015.
[13] Gray RT et al. Estimated contribution of undiagnosed HIV infections among gay and bisexual men to new HIV infections in Australia. Paper presented at Australasian HIV&AIDS Conference, Brisbane 16-18 Sept 2015. **[attached]**