Anti-Infective Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 2 November 2017

(minutes for web publishing)

Anti-Infective Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016.*

Note that this document is not necessarily a complete record of the Anti-Infective Subcommittee meeting; only the relevant portions of the minutes relating to Anti-Infective Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Anti-Infective Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes will be reviewed by PTAC at its meeting on 8 & 9 February 2018, the record of which will be available in due course.

Record of the Anti-Infective Subcommittee meeting held at PHARMAC on 2 November 2017

1 Pre-exposure prophylaxis for prevention of HIV (PrEP)

Background

1.1 The Subcommittee reviewed a funding application from the New Zealand AIDS Foundation to widen funding of tenofovir disoproxil with emtricitabine (TD/FTC) for HIV pre-exposure prophylaxis (PrEP).

Recommendation

1.2 The Subcommittee **recommended** that tenofovir disoproxil with emtricitabine (TD/FTC) be listed on the Pharmaceutical Schedule with a high priority for pre-exposure prophylaxis (PrEP) for individuals at a high risk of contracting HIV.

Discussion

1.3 The Subcommittee reviewed the clinical trial data of TD/FTC for PrEP in the following studies:

- Grant et al. N Engl J Med. 2010; 363(27):2587-99,
- Baeten JM et al. N Engl J Med. 2012;367(5):399-410,
- Baeten JM et al. Lancet Infect Dis. 2014;14(11):1055-64,
- McCormack et al. Lancet. 2016;387(10013):53-60, and
- Molina et al. N Engl J Med. 2015;373(23):2237-46.

The Subcommittee also considered information provided in a Cochrane Review on Antiretroviral PrEP for preventing HIV in high-risk individuals (Owkwundu et al. The Cochrane Library, 2012).

1.4 The Subcommittee considered that there was good quality evidence to support the use of TD/FTC for PrEP to prevent infection in individuals at a high risk of contracting HIV. The Subcommittee noted that the relevant clinical trial data indicated that that daily TD/FTC reduced the relative risk of acquiring HIV infection by 44-86% compared with placebo or no prophylaxis. Members noted that the risk reduction was not very high in the IPrEX study (Grant et al. N Engl J Med. 2010; 363(27):2587-99), but was significantly higher in more recent studies. Members noted that efficacy was strongly correlated to adherence to TD/FTC and in a sub-study of the IPrEX trial, the protective efficacy of PrEP increased to over 96% for those with TD/FTC levels suggested that they took at least 4 doses per week (Anderson et al. Sci Trans Med, 2012).

1.5 The Subcommittee discussed the Auckland Sexual Health Service PrEP Trial, an open-label, single-arm evaluation study run by Dr. Sunita Azariah in Auckland that is still in progress. Enrolments for the trial started in February 2017, and currently 145 of the 150

planned participants have been enrolled. Members noted the inclusion criteria for the trial which was targeted towards gay or bisexual men at a high-risk of contracting HIV. Members noted that rates of sexual transmitted infections were high in participants, and 23% had an STI at enrolment. No HIV seroconversion have been observed to date (unpublished data).

1.6 The Subcommittee considered that there were no other medical treatment options for HIV PrEP. Members considered that while condoms might be considered an alternative, attitudes regarding condoms have changed since HIV is now considered a treatable disease. Members noted that despite the toolbox of strategies available for reducing HIV transmission in New Zealand, including condoms, post-exposure prophylaxis, and early treatment of HIV following diagnosis, new HIV diagnosis rates have been increasing and 2016 saw the highest number of new diagnosis ever in New Zealand. The Subcommittee considered that TD/FTC for PrEP would provide benefit if used by those individuals that do not regularly use condoms and are at a high-risk of contracting HIV.

1.7 The Subcommittee reviewed the groups of individuals considered at a high risk of contracting HIV according to PrEP clinical trial inclusion criteria, the Auckland Sexual Health Service PrEP Trial and the clinical guidelines proposed by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) (Wright et al. J Vir Erad. 2017;3(3):168). Members noted that men who have sex with men (MSM) and women who are regular sexual partners of an HIV positive person (not on treatment and/ or with detectable viral load) with whom condoms have not been consistently used were considered at high risk.

1.8 The Subcommittee discussed the risks and benefits of an open listing. Members considered that an open listing would attract interest from people who had no risk or were at a low–medium risk and were anxious regarding their risk of contracting HIV infection. The Subcommittee noted that restricted access would help in the management of patient's sexual health and in many cases, unnecessary concern regarding their risk of HIV infection. Members emphasised that benefit of PrEP would be best realised, including lower rates of infection for the individual and reduced transmission rates in New Zealand, if access was restricted to individuals that were at a high-risk of infection.

1.9 The Subcommittee considered that should TD/FTC be funded for PrEP, there would not be an increased risk of drug-resistant HIV nor an increased risk of drug-resistance for sexually transmitted infections. Members noted that the risk of selection for drug resistant HIV was more theoretical than real, and cases of drug-resistant HIV detection were in individuals that had an acute HIV infection at the time of enrolment in PrEP. Members noted that commencement on PrEP could encourage riskier behaviour that could increase the rates of sexually transmitted infections. The Subcommittee considered that a requirement for 3-monthly screens for sexually transmitted infections for eligibility for PrEP would mean that patients would be tested and treated more often, reducing the risk of spreading asymptomatic sexually transmitted infections. Members noted that in the longer term there may be an opportunity to reduce STI rates, and associated costs, through early detection and treatment. Members had no concerns regarding the risk of further complications, including renal impairment or bone density loss for patients on daily TD/FTC for PrEP.

1.10 The Subcommittee considered that the cost utility analysis would be highly dependent on HIV incidence rates and noted that in Auckland DHB, the incidence in MSM is estimated at 0.2 per 100 person years. Members noted that TD/FTC would be cost effective if PrEP eligibility was restricted to individuals at a high risk of infection [note part of this text has been redacted].

1.11 The Subcommittee noted that a number of generic emtricitabine with tenofovir disoproxil products that are indicated for PrEP are registered with Medsafe. Members did not express any concern regarding the use of different salt forms of tenofovir disoproxil, and suggested that PHARMAC staff check the current registration of generic tenofovir disoproxil salt forms indicated for PrEP in Europe.

1.12 Members noted that there would be an increase in the resource requirements in sexual health clinics. The Subcommittee considered that monitoring of sexually transmitted diseases would increase testing volumes in laboratories, but this would be relatively low number overall and unlikely to have an appreciable impact.

1.13 The Subcommittee considered that the New Zealand AIDS Foundation estimate of 4000 patients that would be considered at a high-risk of HIV infection and therefore eligible for PrEP was a good estimate.

1.14 The Subcommittee considered that initial treatment should be restricted to, or on the recommendation of, sexual health physicians and infectious disease specialists, and considered that renewals could be prescribed by general practitioners trained in the prescribing and management of patients on TD/FTC for PrEP.

1.15 Members considered that funded access to PrEP be restricted to MSM, or transgender females, are HIV negative and in the last three months met any of the following: are likely to have multiple episodes of receptive condomless anal intercourse, have a regular partner with HIV infection (either not on treatment or with a detectable HIV viral load), have had at least one episode of receptive condomless anal intercourse with a casual male partner, have had a diagnosis of rectal chlamydia/gonorrhoea or any infectious syphilis, have used methamphetamine. The Subcommittee agreed with international guidelines suggesting that individuals that use methamphetamine are considered at a higher risk of contracting HIV due to a number of reasons, including increasing risky behaviour, the higher prevalence of methamphetamine use in MSM and risk associated with needle sharing.

1.16 The Subcommittee also recommended that approvals be valid for three months, with a requirement that patients undergo laboratory testing for HIV, syphilis, a full STI screen and renal testing to qualify for renewal. Members also considered that patients be counselled regarding ways to reduce their risk of contracting HIV. Members noted that PHARMAC would liaise with appropriate Subcommittee members following the meeting to refine Special Authority criteria.