

**4.01 TENOFOVIR with EMTRICITABINE,
Tablet containing tenofovir disoproxil fumarate
300 mg with emtricitabine 200 mg,
Truvada®, Gilead Sciences Pty Ltd.**

**Tablet containing tenofovir disoproxil maleate 300 mg
with emtricitabine 200 mg,
Tenofovir Disoproxil Emtricitabine Mylan 300/200®,
Alphapharm Pty Ltd. (trading as Mylan)**

**Tablet containing tenofovir disoproxil phosphate
291 mg with emtricitabine 200 mg,
Tenofovir EMT GH®, Generic Health Pty Ltd.**

1 Purpose of Application

- 1.1 At its July 2017 meeting, the PBAC considered and deferred two applications for formulations of tenofovir with emtricitabine for Human Immunodeficiency Virus (HIV) Pre-exposure prophylaxis (PrEP), and requested additional analyses for the cost-effectiveness model developed by the Kirby Institute, which was provided as part of both applications.
- 1.2 The PBAC Secretariat engaged with the Kirby Institute to obtain these analyses on behalf of the PBAC. The outcomes of these additional analyses are presented below.
- 1.3 Subsequent to the deferral of the Truvada® and Alphapharm brands, Generic Health Pty Ltd made a submission to the PBAC for its brand of tenofovir with emtricitabine for PrEP, which is PBS listed for the treatment of HIV infection.

2 Requested listing

- 2.1 The PBAC advised at its July 2017 meeting that it was appropriate for an eligible

population to include medium and high risk individuals as defined in the PrEP guidelines published by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM). The listing requested in the July 2017 Truvada® submission (item 7.08), and a summary of the HIV risk criteria for eligibility for PrEP from the ASHM Guidelines, are presented below. For ease of reference, all brands requesting reimbursement of tenofovir with emtricitabine for PrEP at time of PBAC consideration are included in the requested listing below. The risk criteria presented in the ASHM Guidelines are based on sexual and/or drug injecting activity (based on behaviour, not identity) over the last 3 months, and likely activity in the next 3 months (indicating sustained risk). The criteria apply to men who have sex with men (MSM), trans and gender diverse people, heterosexual people and people who inject drugs (PWID).

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
TENOFOVIR DISOPROXIL FUMARATE 300 MG + EMTRICITABINE 200 MG ORAL TABLET, 30	1	2	TRUVADA®	Gilead Sciences Pty Ltd
TENOFOVIR DISOPROXIL MALEATE 300 MG + EMTRICITABINE 200 MG ORAL TABLET, 30	1	2	Tenofovir Disoproxil Emtricitabine Mylan 300/200®	Alphapharm Pty Ltd (trading as Mylan Australia)
TENOFOVIR DISOPROXIL PHOSPHATE 291 MG + EMTRICITABINE 200 MG ORAL TABLET, 30	1	2	Tenofovir EMT GH®	Generic Health Pty Ltd

Category / Program:	General Schedule
PBS Indication:	Pre-exposure prophylaxis against HIV in adults at medium to high risk of infection
Restriction:	Authority Required (STREAMLINED)
Treatment criteria:	Must be treated by a prescriber who is registered with a PrEP Prescriber Program
Clinical criteria:	Patient must be at medium to high risk of HIV infection, as defined by updated Australian Society for HIV Medicine Guidelines. AND Patient must return a negative HIV test prior to initiating treatment AND Patient must continue to return negative HIV tests at 3 monthly intervals throughout treatment.
Population criteria:	Patient must be 18 years or older

Table 1: Risk criteria for MSM to identify their eligibility for PrEP

A. High risk – recommend prescribing daily PrEP if the patient acknowledges		
Having had any of the following in the last 3 months: <ul style="list-style-type: none"> • At least one episode of condomless anal intercourse (CLAI) with a regular HIV+ partner (not on treatment and/or detectable viral load) • At least one episode of receptive CLAI with any casual HIV + male partner or a male partner of unknown status • Rectal gonorrhoea, rectal chlamydia or infectious syphilis diagnosis (during the last 3 months or at screening for PrEP) • Methamphetamine use, which may increase the risk of HIV acquisition 	AND	Being likely to have in the next 3 months (indicating sustained risk): <ul style="list-style-type: none"> • Multiple events of CLAI, with or without sharing intravenous drug equipment
B. Medium risk – consider prescribing daily PrEP, based on case by case approach if discussion reveals		
Having had any of the following in the last 3 months <ul style="list-style-type: none"> • More than one episode of anal intercourse when proper condom use was not achieved (e.g. condom slipped off or broke) where the serostatus of partner was no known, or was HIV+ and not on treatment with a detectable viral load • (if patient uncircumcised) more than one episode of insertive CLAI where the serostatus of partner was not known, or was HIV + and not on treatment or with a detectable viral load 	AND	Being likely to have in the next 3 months (indicating sustained risk) <ul style="list-style-type: none"> • Multiple events of CLAI, with or without sharing intravenous drug equipment
<p>Case by case approach Based on a complete sexual and alcohol and other drug-using history and the personal circumstances of the patient, if the clinician is of the opinion that the patient is likely to be at high risk of HIV, then PrEP prescription may be considered despite the absence of reported high- or medium-risk factors above.</p>		

Source: Wright, Edwina, et al. Australasian Society for HIV, Viral Hepatitis, and Sexual Health Medicine - HIV Pre-Exposure Prophylaxis: clinical guidelines. Journal of Virus Eradication, 2017; 3: 168-184. Accessed 5 July 2017. Open access, available at http://viruseradication.com/journal-details/Australasian_Society_for_HIV,_Viral_Hepatitis_and_Sexual_Health_Medicine_HIV_pre-exposure_prophylaxis:_clinical_guidelines/

2.2 The PBAC considered at its July 2017 meeting that tenofovir with emtricitabine for PrEP should be listed as a General Schedule item to ensure widest access and should include provision for nurse practitioner prescribing.

2.3 The PBAC considered at its July 2017 meeting that the proposed maximum quantity and number of repeats, which provides for up to 3 months' treatment, is appropriate and reflects the need for frequent review of patient circumstances, including their risk profile and HIV infection status. The PBAC noted the increase in the reported cases of sexually transmitted infections (STIs) in the clinical studies of PrEP and considered in clinical practice, the requirement of a medical practitioner visit every 3 months to obtain a prescription for tenofovir with emtricitabine is likely to increase monitoring for STIs and result in earlier diagnosis.

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Background

3.1 The Truvada® brand of tenofovir with emtricitabine was recommended by the PBAC in November 2005 and PBS listed on 1 April 2006 for the treatment of HIV infection. This brand of tenofovir with emtricitabine was TGA registered for use 'in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk' on 6 May 2016. The PBAC previously considered submissions for PrEP for the Truvada® brand at its July 2016 and July 2017 meetings.

3.2 The Tenofovir Disoproxil Emtricitabine Mylan 300/200® brand of tenofovir with emtricitabine was TGA registered on 10 April 2017 for:

- the treatment of HIV infected adults over the age of 18 years, in combination with other antiretroviral agents; and
- in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

This brand of tenofovir with emtricitabine was PBS listed on 1 August 2017 for the treatment of HIV infection. The PBAC previously considered a minor submission for this brand of tenofovir with emtricitabine for PrEP at its July 2017 meeting.

3.3 The Tenofovir EMT GH® brand of tenofovir with emtricitabine was TGA registered on 31 January 2017 for:

- The treatment of HIV infected adults over the age of 18 years, in combination with other anti-retroviral agents; and
- In combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

This brand of tenofovir with emtricitabine was PBS listed on 1 August 2017 for the treatment of HIV infection, as an additional brand.

3.4 Key aspects of the PBAC's consideration of PrEP at its July 2017 meeting included:

- The PBAC reaffirmed it accepted standard of care (SOC), as a combination of other safe sex practices, as the appropriate comparator.
- The PBAC accepted, based on the evidence presented in the submissions, that tenofovir with emtricitabine as PrEP appeared to be effective in reducing the transmission of HIV.

- The PBAC reaffirmed its previous advice that it considered the claim of non-inferior comparative safety was not strongly supported by the available data, however given the duration of experience with tenofovir with emtricitabine for the treatment of HIV, that the claim of non-inferior comparative safety was probably reasonable.
- The PBAC considered that the economic model developed by the Kirby Institute assessing the cost-effectiveness of PrEP in MSM was more likely to accurately predict HIV incidence and prevalence than the economic model provided in the Truvada® submission given the modelling and calibration approaches used. In addition, the shorter time horizon for the Kirby model (14 years vs. 20 years) reduced the uncertainty associated with the estimates.

3.5 The results for the Kirby model were presented for a number of scenarios based on different uptake in individuals at high, medium or low risk of infection. The uptake scenarios ranged from 30-0-0 (30% uptake in high risk, 0% in medium risk, 0% in low risk; 8.4% overall uptake) to 90-90-90 (90% overall uptake). The PBAC noted in July 2017 that only two of the scenarios presented considered use only in individuals at high and medium risk of infection. Further, both of the scenarios assumed 90% uptake in high risk individuals and the PBAC considered that this level of uptake was unlikely to be achieved in clinical practice. The PBAC considered alternative scenarios assuming lower uptake in medium and high risk individuals would be informative.

3.6 For the Kirby model, the annual PrEP cost required for the cost per QALY gained to be \$30,000, \$60,000 or \$90,000 was presented. In July 2017, the PBAC recalled that the threshold of incremental QALYs gained for treatments with large opportunity costs, such as population preventative interventions including lipid-lowering, anti-hypertensive drugs and vaccines, was at the lower end of the ICER range that PBAC has accepted because these treatments typically have a high opportunity cost. Though not completely analogous to a vaccination program such as against Human Papillomavirus (HPV), the PBAC considered that subsidisation of PrEP, like the HPV vaccine, would provide both direct benefits to the treated individual and wider benefits to society with reductions in the prevalence of HIV infection over time. The PBAC considered that the acceptable ICER for PrEP should be at the low end of the range previously accepted for these other population preventative interventions with large opportunity costs. Thus the PBAC considered alternative scenarios considering ICER thresholds below \$30,000 per QALY gained would be informative.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item. The PBAC were reminded of the large volume of supportive consumer comments received and discussed at the July 2017 meeting.

Economic Analysis

- 4.3 The results for the following additional analyses were provided by the Kirby Institute:
- Uptake in 40%, 50%, 60%, 70% and 80% of the eligible high and medium risk populations.
 - The annual cost of PrEP required for ICER thresholds of \$10,000, \$15,000, \$20,000 and \$25,000 per QALY gained.
- 4.4 The Kirby Institute advised that in the process of preparing the additional analyses, an error was identified in the costing calculations for providing PrEP for the specified coverage in each scenario. The error resulted in PrEP costs and the resulting ICER being over-estimated by 10-20% in the original analysis, and the PrEP unit cost being required to meet the cost-effectiveness thresholds being underestimated by a similar margin. The corrected results and the additional results are presented in Tables 2, 3 and 4. The results in Table 2 are based on a monthly cost for tenofovir with emtricitabine of \$788.57 (the dispensed monthly price of Truvada® at 1 January 2016) which is equivalent to an annual cost of \$9,605.

Table 2: Results of Kirby Economic Model: cost per QALY gained for different uptake scenarios based on an annual PrEP cost of \$9,605

Scenario (uptake in high, medium and low risk)	Infections averted	QALYs gained (discounted)	Incremental costs (discounted)	Cost per QALY gained
Uptake scenarios considered at July 2017 PBAC meeting - corrected				
30-0-0	4720	2190	\$145,542,900	\$70,470
60-0-0	7790	3830	\$354,446,840	\$100,850
90-0-0	9540	4940	\$607,931,070	\$133,240
90-20-0	9580	4960	\$644,440,760	\$140,820
90-60-0	9650	5010	\$720,706,150	\$155,040
90-20-10	9830	5130	\$1,015,271,360	\$202,820
90-60-30	10350	5460	\$1,805,259,340	\$328,290
90-90-90	11330	6270	\$3,964,568,070	\$620,600
Additional uptake scenarios				
40-40-0	6060	2880	\$285,740,950	\$104,330
50-50-0	7090	3430	\$376,715,130	\$115,730
60-60-0	7940	3920	\$472,352,900	\$127,550
70-70-0	8650	4340	\$572,002,020	\$139,960
80-80-0	9230	4720	\$675,112,680	\$152,650

Source: Kirby Institute and the Centre for Social Research in Health (October 2017). Discussion paper: Updated Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness. Appendix, Table A6. Source: Kirby Institute and the Centre for Social Research in Health (October 2017). Discussion paper: Updated Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness. Addendum, Table 3.

Table 3: PrEP annual cost required for scenario to be cost-effective for a given willingness-to-pay threshold (A\$ per QALY gained). For each scenario and cost-effectiveness threshold, the table shows the median value from the simulation ensemble. Corrected results for analyses considered at July 2017 meeting.

Scenario	\$30,000 per QALY gained	\$60,000 per QALY gained	\$90,000 per QALY gained
30-0-0	\$7,090	\$9,440	\$11,770
60-0-0	\$5,790	\$7,690	\$9,580
90-0-0	\$4,870	\$6,450	\$8,020
90-20-0	\$4,720	\$6,230	\$7,730
90-60-0	\$4,430	\$5,830	\$7,230
90-20-10	\$3,620	\$4,780	\$5,930
90-60-30	\$2,430	\$3,210	\$3,990
90-90-90	\$1,440	\$1,890	\$2,340

Source: Kirby Institute and the Centre for Social Research in Health (October 2017). Discussion paper: Updated Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness, Table A7, p 38.

Table 4: PrEP annual cost required for scenario to be cost-effective for a given willingness-to-pay threshold (A\$ per QALY gained). For each scenario and cost-effectiveness threshold, the table shows the median value from the simulation ensemble. Results for additional uptake scenarios and cost-effectiveness thresholds.

Scenario	\$10,000/QALY	\$15,000/QALY	\$20,000/QALY	\$25,000/QALY	\$30,000/QALY
40-40-0	\$4,450	\$4,760	\$5,060	\$5,370	\$5,680
50-50-0	\$4,180	\$4,470	\$4,760	\$5,040	\$5,330
60-60-0	\$3,940	\$4,210	\$4,480	\$4,750	\$5,020
70-70-0	\$3,720	\$3,970	\$4,220	\$4,470	\$4,720
80-80-0	\$3,510	\$3,750	\$3,990	\$4,220	\$4,460

Source: Kirby Institute and the Centre for Social Research in Health (October 2017). Discussion paper (appendum): Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness, Table 4, p 4.

- 4.5 The ICER increases as the uptake of PrEP increases, reflecting diminishing returns as the number of individuals using PrEP increases, particularly when extended to medium and low risk individuals (Table 2).
- 4.6 Assuming 40% uptake in high and medium risk individuals, and an annual PrEP cost of \$9,605, the cost per QALY gained is \$104,330. If uptake is increased to 80%, the ICER increases to \$152,650 per QALY gained.
- 4.7 As noted in the July 2017 PBAC minutes the proposed eligibility criteria (see Table 1) rely on self-reported behaviour. Thus there is the potential for use in a proportion of individuals at low risk of infection. The impact on the cost-effectiveness of PrEP use in low risk individuals can be assessed by comparing scenario 90-20-0 with 90-20-10 (i.e 10% uptake in low risk individuals) and scenario 90-60-0 with 90-60-30 (i.e 30% uptake in low risk individuals). Uptake of 10% in low risk individuals increases the ICER by 44% (\$202,820 vs \$140,820). Uptake of 30% in low risk individuals increases the ICER by 112% (\$155,040 vs \$328,290).
- 4.8 For the scenario 40-40-0 (the lowest uptake assessed), the annual cost of PrEP would need to be \$4,450 for the cost per QALY gained to be \$10,000, increasing to an annual cost of \$5,680 for the cost per QALY gained to be \$30,000 (Table 4).
- 4.9 For the scenario 80-80-0, the annual PrEP cost would need to be \$3,510 for the cost per QALY gained to be \$10,000, increasing to an annual cost of \$4,460 for the cost per QALY gained to be \$30,000 (Table 4).
- 4.10 The impact of use in low risk individuals on the PrEP cost required to meet a specific cost/QALY threshold can be assessed by comparing scenario 90-20-0 with 90-20-10 (i.e 10% uptake in low risk individuals) and scenario 90-60-0 with 90-60-30 (i.e 30% uptake in low risk individuals). For a specified ICER, the annual PrEP cost needs to be reduced by 23% if there is use in 10% of low risk individuals (eg for an ICER of \$30,000 the annual PrEP cost needs to be reduced from \$4,720 to \$3,620 if there is use in 10% of low risk individuals, Table 3). For a specified ICER, the annual PrEP cost needs to be reduced by 45% if there is use in 30% of low risk individuals (eg for an ICER of \$30,000 the annual PrEP cost needs to be reduced from \$4,430 to \$2,430 if there is use in 30% of low risk individuals, Table 3).
- 4.11 Further information on the context of these analyses is available in the relevant Public Summary Documents for tenofovir with emtricitabine (items 6.16 and 7.08) from the July 2017 PBAC meeting.

- 4.12 Generic brands have now been listed for tenofovir with emtricitabine. Although not a matter for the PBAC, it is noted that any PBS listings for the PrEP indication will be subject to price disclosure from the time tenofovir with emtricitabine moved to the F2 formulary (1 August 2017).

Estimated PBS usage & financial implications

- 4.13 The total number of person years of PrEP by calendar year as estimated from the Kirby model are presented in Table 5. These estimates are based on:
- A total gay male population in 2015 of 123,600 individuals, of which 38,200, 5,100 and 80,300 are high, medium and low risk, respectively;
 - 19,067 MSM living with HIV in 2016 and hence not eligible for PrEP;
 - Uptake as specified in Table 5 ranging from 40% in high and medium risk individuals to 80% in high and medium risk individuals;
 - 90% adherence with PrEP; and
 - Scale up of the PrEP program over three years.

Table 5: Total number of person-years of PrEP use each year. Median and range for the 50 model simulations for the number of person-years HIV-negative gay men take PrEP each year accounting for coverage, adherence (90%), a 3-year scale-up to reach the specified coverage, and population growth.

PrEP usage scenario	2016	2017	2018	2019	2020	2021	2022	2023	2024
Scenario 40-40-0	1,850 (1,150- 2,680)	5,120 (3,000- 7,360)	8,470 (4,920-12,200)	10,620 (6,160-15,290)	10,830 (6,290-15,580)	11,050 (6,420-15,880)	11,274 (N/A)	11,503 (N/A)	11,737 (N/A)
Scenario 50-50-0	2,200 (1,340- 3,170)	6,330 (3,700- 9,100)	10,580 (6,140-15,230)	13,330 (7,730-19,170)	13,610 (7,910-19,560)	13,910 (8,090-19,970)	14,217 (N/A)	14,530 (N/A)	14,850 (N/A)
Scenario 60-60-0	2,540 (1,540- 3,650)	7,540 (4,400-10,830)	12,700 (7,370-18,270)	16,050 (9,310-23,070)	16,420 (9,540-23,570)	16,810 (9,780-24,090)	17,209 (N/A)	17,618 (N/A)	18,036 (N/A)
Scenario 70-70-0	2,890 (1,740- 4,140)	8,750 (5,100-12,570)	14,830 (8,610-21,320)	18,790 (10,900-27,000)	19,260 (11,190-27,620)	19,730 (11,480-28,250)	20,211 (N/A)	20,705 (N/A)	21,210 (N/A)
Scenario 80-80-0	3,240 (1,930- 4,630)	9,960 (5,800-14,310)	16,960 (9,840-24,380)	21,550 (12,510-30,940)	22,110 (12,850-31,680)	22,680 (13,200-32,430)	23,265 (N/A)	23,864 (N/A)	24,480 (N/A)

Source: Kirby Institute and the Centre for Social Research in Health (October 2017). Discussion paper (appendum): Estimates of the number of people eligible for PrEP in Australia, and related cost-effectiveness, Table 2, p 3. Person-years of PrEP in 2022-2024 estimated by the PBAC Secretariat and assume annual growth is the same as for 2020 to 2021 (i.e. 2.0% for 40% uptake, 2.2% for 50% uptake, 2.4% for 60% uptake, 2.4% for 70% uptake and 2.6% for 80% uptake). Ranges not estimated for period 2022-2024.

- 4.14 From 2019 onwards (following the assumed 3 year scale up period), there are approximately 11,000 person years of PrEP based on uptake of 40% in high and medium risk individuals and 22,000 person years of PrEP based on uptake of 80% (Table 5).
- 4.15 The assumed adherence of 90% may be high given in clinical practice intermittent use of PrEP is likely in a proportion of individuals. Intermittent PrEP use would reduce the total use and hence cost of PrEP. Conversely, use in low risk individuals would increase the total use and costs of PrEP.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of tenofovir with emtricitabine for human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP). The PBAC was satisfied that tenofovir with emtricitabine provides, for some patients, a significant reduction in the risk of sexually-acquired HIV when used in combination with the promotion of other safe sex practices, compared with the promotion of other safe sex practices alone. The PBAC's recommendation for listing was based on, among other matters, its assessment of the cost-effectiveness of PrEP based on the model developed by the Kirby Institute.
- 5.2 In response to the request from the Minister (delegate) under section 101(3) of the *National Health Act 1953* ('the Act'), the PBAC considered the price or range of prices at which it considered treatment with tenofovir with emtricitabine as PrEP would be acceptably cost-effective for the purposes of the Act. The PBAC advised that the maximum price it would consider to be acceptably cost-effective, noting the price and incremental cost-effectiveness ratios (ICERs) of other large population preventive interventions such as lipid lowering medicines and vaccines on the National Immunisation Program (NIP) would be an annual treatment cost of \$2,500 per patient per year. This is equivalent to a DPMQ of approximately \$205 per pack of 30 tablets.
- 5.3 The PBAC noted the cost-effectiveness of PrEP was dependent on the extent of uptake and the risk profile of the individuals who use PrEP. Specifically, as demonstrated in Table 2 above, the ICER increases as the uptake of PrEP increases, reflecting diminishing returns as the number of individuals using PrEP increases, particularly when extended to medium and low risk individuals.
- 5.4 Regarding the likely uptake of PrEP, the PBAC noted evidence of substantial awareness and familiarity of PrEP amongst sexually active gay men; however a reasonable proportion of the total (approximately 30%) of that population did not

indicate a willingness to use PrEP^{1,2}. The PBAC considered that individuals at higher risk of acquiring HIV were more likely to be willing to use PrEP.

- 5.5 The PBAC noted an update on the uptake of PrEP in the state-based trials³ and demonstration projects, and that as at November 2017, approximately 14,000 people were enrolled and on treatment and that this represented approximately half of the estimated MSM population at high risk of sexually-acquired HIV. These projects are continuing to recruit with 85% uptake considered the likely maximum enrolment. The PBAC noted that State and Territory Communicable Disease programs and established community groups have successfully run comprehensive health promotion tools and education campaigns over the past several years. The PBAC considered that these programs and the high awareness of PrEP in the target population would deliver an ongoing consistency in prescribing practice and consumer uptake as the medicine transitioned from State access programs to PBS supply.
- 5.6 The PBAC noted in the PrEPx demonstration project only a small proportion of individuals (3.4%) were enrolled based on clinician discretion. The Committee further noted that in the PrEP projects in NSW, Victoria and Queensland there has been no decrease in sexually transmitted infections (STIs) at baseline, suggesting that the projects are continuing to recruit high-risk individuals. Overall, with PrEP access through the PBS, the PBAC considered that there was a risk of some use of PrEP in low risk individuals, or of adoption of higher risk behaviour among previously low and medium risk individuals, but that the extent of use in these individuals would be relatively low.
- 5.7 The PBAC considered the impact of a number of uptake scenarios on the cost-effectiveness of PrEP. The PBAC noted with 80% uptake in high and medium risk individuals (80-80-0) the annual cost of tenofovir with emtricitabine would need to be \$3,750 per patient for the ICER to be \$15,000 per QALY gained. If there was 10% use in low risk individuals, the annual cost would need to be reduced by 23% (to \$2,888 per patient) for the ICER to remain at \$15,000 per QALY gained. The PBAC considered an uptake scenario of 60-60-30 as a likely extreme scenario, and noted for this scenario the ICER would be between \$15,000 and \$30,000 per QALY gained resulting in an annual PrEP cost between \$2,316 ($\$4,210 \times 0.55$) and \$2,464 ($\$4,480 \times 0.55$). Overall, the PBAC advised that tenofovir with emtricitabine for PrEP is likely to

¹ Holt M, Lea T, Schmidt H, *et al*, Willingness to use and have sex with men taking HIV pre-exposure prophylaxis (PrEP): results of online surveys of Australian gay and bisexual men, 2011–2015 *Sex Transm Infect* 2017;93:438-444.

² Prestage G, Maher L *et al* 2017, 'Why are some gay and bisexual men eligible for PrEP but not taking it?', Australasian HIV & AIDS Conference Report of Proceedings, National Convention Centre, Canberra, Australia. [Conference abstract available online.](#)

³ Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM), 2017 Australasian HIV & AIDS Conference Key Learnings Report, pg. 8. Available online at <http://www.hivaidconference.com.au/>

be acceptably cost-effective if the annual treatment cost did not exceed \$2,500 per patient.

- 5.8 The PBAC noted that some individuals not enrolled in state-based PrEP demonstration projects are privately accessing PrEP, primarily from outside Australia under personal importation provisions permitted in the *Therapeutic Goods Regulations 1990*, at a price that is lower than that requested by any of the sponsor companies. The PBAC also noted that since generic brands of tenofovir with emtricitabine are listed on the PBS, the drug is subject to price disclosure and the price will reduce over time, however the magnitude of the price reductions cannot be determined prospectively.
- 5.9 The PBAC noted the estimated extent of use for the financial forecasts was based on the number of HIV negative individuals at high or medium risk of infection, and the uptake (40-80%) and adherence (90%) with PrEP. Based on the uptake in state-based projects and the proportion indicating a willingness to use PrEP, the PBAC considered the uptake of PrEP was likely to be in the order of 60-70% of eligible individuals (i.e. approximately 16,000 to 19,000 individuals in 2019, Table 5). The PBAC noted these estimates did not consider use in low risk individuals and considered that use in these individuals is likely to be relatively low. The PBAC also noted that these estimates did not consider intermittent use in high and medium risk individuals and that this will reduce the extent of use. The Committee recalled from the July 2017 PBAC meeting there was clinical evidence demonstrating the efficacy of intermittent PrEP regimens and considered there would be substantial fluidity in the use of PrEP with many individuals likely to start and stop PrEP as their risk profile changed over time. Overall, the PBAC advised that it considered the Kirby scenario 60-60-0 (Table 5) to be the best available estimate of the uptake and use of PrEP based on the totality of the available evidence.
- 5.10 The PBAC reaffirmed its position that it was appropriate for the ASHM PrEP guidelines to be used as the basis for defining medium and high-risk individuals and that patients should return a negative HIV test prior to commencing PrEP. The PBAC noted that some trials reported a decrease in the use of other safe sex practices, including condom use, and reiterated that PrEP should be used as part of a comprehensive approach to HIV and STI risk reduction that should include continued use of other safe sex practices. The PBAC also noted that the experience of the Australian PrEP programs to date provide evidence that those individuals self-reporting for PrEP assessment are meeting the eligibility criteria that is considered appropriate.
- 5.11 The Committee advised it was appropriate for up to three months' supply to be accessed at a time for PrEP and that individuals should continue to return a negative HIV test before each new three month supply of PrEP. While not a matter related to the listing of PrEP, the PBAC noted that the requirement for patients to return negative HIV tests at regular intervals may present an opportunity for increased

broader sexual health monitoring among people receiving PrEP, which may result in earlier detection and treatment of other STIs.

- 5.12 The PBAC considered the appropriateness of the requested restriction with regard to the need for prescribers to be enrolled in a PrEP prescriber program. The PBAC noted that no such prescriber program currently exists, nor is there any certainty that such a program will exist in the future, and therefore did not recommend that such a requirement be included in the restriction at this time.
- 5.13 The PBAC noted that this recommendation applies only to tenofovir with emtricitabine in the form of tenofovir disoproxil (and its various salts), and not to products containing tenofovir alafenamide.
- 5.14 The PBAC advised that tenofovir with emtricitabine for PrEP is suitable for prescribing by nurse practitioners, however that the Section 100 listings for treatment of HIV infection should remain restricted to medical practitioners, noting that patients receiving tenofovir with emtricitabine for treatment of HIV infection are able to access substantially longer supply through the relevant Section 100 listings.
- 5.15 The PBAC recommended that the Early Supply Rule should apply, similar to existing listings for tenofovir with emtricitabine for the treatment of HIV infection.
- 5.16 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Add new item:

Name, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
TENOFOVIR DISOPROXIL FUMARATE 300 MG + EMTRICITABINE 200 MG ORAL TABLET, 30	1	2	TRUVADA®	Gilead Sciences Pty Ltd
TENOFOVIR DISOPROXIL MALEATE 300 MG + EMTRICITABINE 200 MG ORAL TABLET, 30	1	2	Tenofovir Disoproxil Emtricitabine Mylan 300/200®	Alphapharm Pty Ltd (trading as Mylan Australia)
TENOFOVIR DISOPROXIL PHOSPHATE 291 MG + EMTRICITABINE 200 MG, ORAL TABLET, 30	1	2	Tenofovir EMT GH®	Generic Health Pty Ltd

Category/Program:	General Schedule
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners
Condition:	Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection
PBS Indication:	Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection
Restriction:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>The treatment must be for patients at medium to high risk of HIV infection, as defined by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Guidelines;</p> <p>AND</p> <p>Patient must have a negative HIV test result prior to treatment with PBS-subsidised therapy with this drug.</p>
Population criteria:	Patient must be 18 years or older.
Administrative advice:	<p>No increase in the maximum quantity or number of units may be authorised.</p> <p>No increase in the maximum number of repeats may be authorised.</p>

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

10 Sponsor's Comment

Gilead Sciences Pty Ltd

Gilead welcomes the PBAC's decision to recommend PBS listing of Truvada (tenofovir with emtricitabine) for pre-exposure prophylaxis against HIV infection.

Alphapharm Pty Ltd (trading as Mylan)

The sponsor had no comment.

Generic Health Pty Ltd

The sponsor had no comment.