Agenda item 11.02
TENOFOVIR with EMTRICITABINE,
Tablet containing tenofovir disoproxil fumarate 300 mg with emtricitabine 200 mg,
Tenofovir/Emtricitabine 300/200 APOTEX®,
Apotex 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 Item

1.1 To request PBAC consideration of the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine's (ASHM's) proposed change to Pharmaceutical Benefits Scheme (PBS) prescribing criteria for HIV Pre-Exposure Prophylaxis (PrEP) medications in response to the *2019 ASHM PrEP Guidelines*.[1]

2 Background and current situation

2.1 Tenofovir disoproxil with emtricitabine (TD/FTC) was recommended by the PBAC in December 2017 and PBS listed on 1 April 2018 for PrEP.

2.2 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. 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.

2.3 At its December 2017 meeting, the PBAC advised that it was appropriate for the *2017 ASHM PrEP Guidelines* to be used as the basis for defining medium and high-

[1] Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine HIV pre-exposure prophylaxis: clinical guidelines. September 2019.

risk individuals and that patients should return a negative HIV test prior to commencing PrEP and at 3-monthly intervals during treatment.

2.4 The current restriction for PBS subsidised TD/FTC for PrEP requires patients to be at medium to high risk of HIV infection as defined by the *2017 ASHM Guidelines*.

2.5 The ASHM updated its guidelines in 2019. The *2019 ASHM PrEP Guidelines* no longer propose classification of people into high and medium HIV risk. It recommends that PrEP be prescribed in any situation where there is an identified risk of HIV transmission, including risk that is current or may occur in the near future.

2.6 The price of TD/FTC has decreased by 58%, from an AEMP of $220.34 per pack of 30 at time of listing to $92.49 as of 1 August 2020. These reductions have largely been driven by price disclosure as TD/FTC is in the F2 formulary. The reference brand, Truvada®, was delisted from the PBS in April 2020.

2.7 The annual cost of daily PrEP per patient at the current DPMQ as of 1 August 2020 ($111.47, 12.16 prescriptions/year) equates to $1,355.48 per patient.

December 2017 PBAC Recommendation

2.8 The December 2017 PBAC recommendation was based upon the PBAC's consideration of an economic model developed by the Kirby Institute, which presented cost-effectiveness scenarios for numerous combinations of projected use for the men-who-have-sex-with-men (MSM) population at high, medium or low risk of acquiring HIV at different annual cost thresholds.

2.9 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. Overall, the PBAC advised that tenofovir with emtricitabine for PrEP was likely to be acceptably cost-effective if the annual treatment cost did not exceed $2,500 per patient. This was equivalent to a DPMQ of approximately $205 (an AEMP of ~$180) per pack of 30 tablets. The price of TD/FTC was weighted with its existing HIV treatment indication at time of listing. The PBAC noted the cost-effectiveness of PrEP was particularly sensitive to the proportion of patients defined as having a low risk of acquiring HIV, however considered that use in this group was likely to be low. The below table outlines the annual costs and ICER thresholds for different usage patterns from the Kirby model relied upon in the December 2017 submission.

Table 1: 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. Extracted from the December 2017 Public Summary Document.

2.10 At the current annual treatment cost of daily PrEP ($1,355), the cost effectiveness is below $30,000 per QALY for all scenarios, including Scenario 90-90-90, which assumed 90% of all patients at high, medium or low risk are treated.

3 Consideration of the evidence

ASHM comments on PrEP Use and Impact in Australia

3.1 Australia was one of the first countries in the world to provide access to government subsidised PrEP for people at risk of HIV. The PBS listing of medications for PrEP in April 2018 has likely played a key role in the decline of new HIV notifications, with the annual number of HIV diagnoses in Australia declining by 23% during 2014-2018. This decrease was largely attributable to a 30% decline in HIV notifications among men who have sex with men (MSM).[2]

3.2 Based on data published by the Kirby Institute, at the end of June 2019 it was estimated that 26,520 people were on PrEP in Australia, of whom 98.8% were recognised as male.[3] A 25% decline in new HIV diagnoses was observed among MSM in New South Wales, largely related to PrEP availability and awareness, from 295 in the 12 months before the Expanded PrEP Implementation in Communities New

[2] Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney; 2018. Available at: https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance (last accessed 8 June 2020).

[3] Monitoring HIV pre-exposure prophylaxis uptake in Australia, Issue 1 June 2019. Available at: https://kirby.unsw.edu.au/sites/default/files/kirby/report/Monitoring-HIV%20pre-exposure-prophylaxis-in-Australia-newsletter_Issue-2.pdf (last accessed 8 June 2020).

South Wales (EPIC-NSW) study commenced to 221 in the 12 months following study commencement.[4]

3.3 The ASHM noted the latest estimate from the Kirby Institute shows that around 26,360 people throughout Australia were taking PrEP at some time during the three months to 31 March 2020. A comparison between 2019 and 2020 PrEP uptake figures indicates that PrEP uptake appears to have slowed, notwithstanding that there have been ongoing governmental and community PrEP awareness campaigns.

3.4 ASHM also stated that PBS costs for PrEP may have been considerably lower than predicted by the Department of Finance at the time of PBS listing of PrEP (1 April 2018), indicating a slowing of PrEP uptake and continuation.

3.5 At this time, a key target of Australia's National HIV Strategy target, which is to increase the proportion of eligible people taking PrEP to 75 per cent by 2022, may not be met. The ASHM considered the impact of the COVID-19 pandemic on PrEP use is unknown, but there are anecdotal reports that there are impacts on PrEP use, including reluctance among some people to seek medical care because of the pandemic.

PBS Utilisation of PrEP since April 2018

3.6 To examine the use of PrEP on the PBS, data were extracted from Services Australia Supplied Prescription Database on the utilisation of PrEP for the period 1 April 2018 to 30 June 2020.

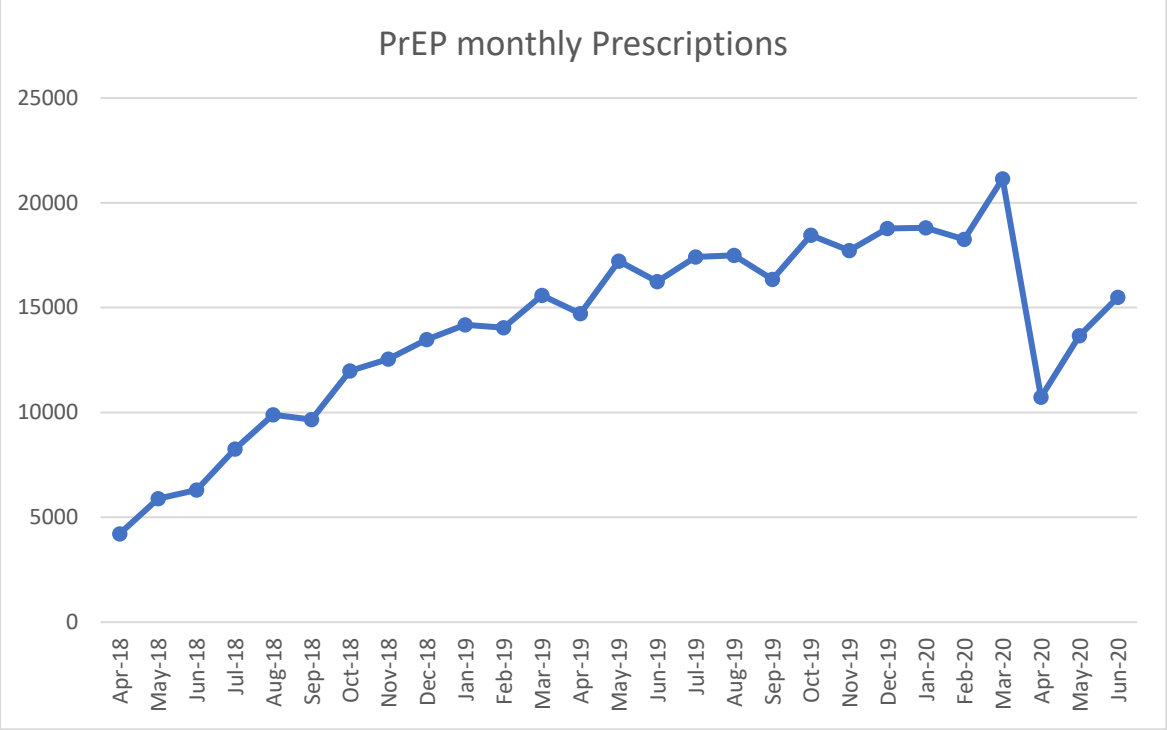
3.7 Over that period, the number of patients supplied PrEP in a calendar month increased from 1,920 (4,217 scripts) in April 2018 to a peak of 12,669 (21,149 scripts) in March 2020. The PBAC noted the number of PrEP prescriptions was lower than the estimates in the December 2017 submission.

3.8 There was a sharp decrease in the number of supplied prescriptions and patients in April 2020 and subsequent months, which was preceded by an off-trend increase in prescribing in March 2020, aligning with the announcement and commencement of COVID-19 related public health measures and restrictions.

3.9 Utilisation statistics by month (prescription counts and patient counts) from the date of listing are presented in the Figure 1 and Figure 2.

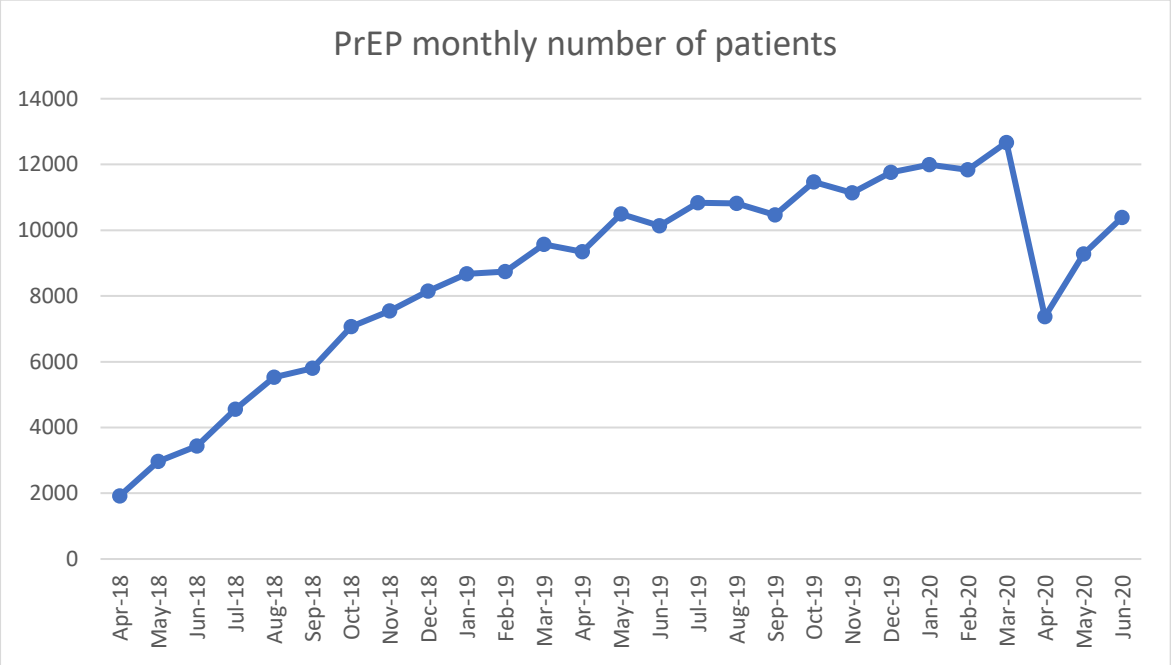
[4] Grulich AE, Guy R, Amin J, et al; Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) research group. Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. Lancet HIV 2018;5:e629-37.

Figure 1: Monthly PrEP prescriptions dispensed 1 April 2018 - 30 June 2020



Source: Services Australia supplied prescription database, extracted 20 August 2020. Combined total of all brands/forms of tenofovir with emtricitabine dispensed under PrEP PBS item codes

Figure 2: Monthly number of patients dispensed PBS-subsidised PrEP 1 April 2018 - 30 June 2020



Source: Services Australia supplied prescription database, extracted 20 August 2020. Combined total of all brands/forms of tenofovir with emtricitabine dispensed under PrEP PBS item codes.

3.10 For the only full calendar year for which PrEP has been listed on the PBS (2019), Commonwealth benefits paid for PrEP was $30,204,524.[5]

4 ASHM Comments on simplifying PBS Prescribing Criteria for PrEP

4.1 Since PBS availability of PrEP in April 2018, ASHM has sought to streamline the information provided to clinicians and patients about PrEP wherever possible. The ASHM advised the 2017 PrEP guidelines contained some complex assessment criteria, which from anecdotal reports, were a disincentive to some patients to ask about PrEP and for some clinicians to prescribe it; especially in low HIV caseload settings and/or among patients with diverse cultural and linguistic backgrounds or who may be marginalised in other ways.

4.2 The 2017 ASHM PrEP guidelines classified a person's risk of HIV acquisition as high or low based on criteria from Poynten et al., 2010.[6] The 2017 guidelines recommended that an individual had to report HIV risk in the 3 months before commencing PrEP and that the individual anticipated that they would have HIV risk in the 3 months after commencing PrEP. Additionally, in the 2017 guidelines, clinicians were invited to consider offering PrEP on a case-by-case basis to people who did not meet high or medium risk criteria.

4.3 Reflecting the need to minimise complexity, the 2019 ASHM PrEP guidelines no longer classify a person's risk of HIV acquisition as high or low and no longer require that an individual demonstrate HIV risk in the previous 3 months. Instead the 2019 guidelines provide behavioural examples of what would make a person suitable for PrEP, including whether a person's quality of life would likely improve if they were offered PrEP, e.g. people with high levels of anxiety about HIV acquisition.

4.4 The ASHM argued the current epidemiological data highlight the need to strengthen the current strategies for HIV prevention in Australia, especially in Indigenous populations, overseas-born MSM where HIV rates are rising, and heterosexuals, which would include expanding the uptake of PrEP by all eligible people at risk. The PrEP suitability eligibility criteria that are provided in these guidelines are not intended to limit or deny access to PrEP to any person who seeks it. Instead, they are intended to help identify and actively recommend PrEP to people suitable for PrEP and to guide clinicians in their discussions about PrEP with patients who are uncertain about their HIV risk and need for PrEP use.

[5] Extracted 20 August 2020 from publicly available data on the Medicare Statistics website at http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp

[6] Poynten IM, Jin F, Prestage GP, Kaldor JM, Kippax S, Grulich AE. Defining high HIV incidence subgroups of Australian homosexual men: implications for conducting HIV prevention trials in low HIV prevalence settings. HIV Med 2010;11:635-41. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1468-1293.2010.00833.x (last accessed 26 August 2020)

4.5 The 2019 ASHM PrEP Guidelines also support the use of intermittent/on demand PrEP only for the cis-gender[7] MSM population, and only for those who do not have chronic hepatitis B (CHB) and are engaging in sexual activity less than twice a week, where such activity is unpredictable and can be delayed by at least two hours. The Guidelines were informed by clinical studies which indicated that in cis-gender women, PrEP does not achieve adequate levels in tissues to be considered effective when taken intermittently. Intermittent/on demand PrEP was not considered suitable for those engaging in frequent at-risk activities and for those with CHB due to the risk of disease flare.

5 Requested change in PBS Prescribing Criteria for PrEP

5.1 The ASHM requested that the PBAC consider changing the clinical criteria for prescribing PrEP medication under the PBS to accord with the criteria recommended in the 2019 ASHM PrEP Guidelines, including the reference to medium or high risk and to remove current age restrictions to allow greater flexibility in the listing.

6 PBAC Outcome

6.1 The PBAC recommended the continued PBS listing of tenofovir disoproxil with emtricitabine (TD/FTC) for pre-exposure prophylaxis (PrEP) against HIV infection and further recommended the restriction level be reduced to a Restricted Benefit to support broad access for patients who are at risk of HIV infection.

6.2 In making this recommendation, the PBAC considered the guidelines and additional training provided by the ASHM, as a peak clinical organisation in this field, provide an adequate framework for PrEP prescribing that is likely to result in the cost-effective use of PrEP in the context of:

- the level of price reduction since listing and current price of TD/FTC on the PBS (and possible future price reductions due to price disclosure);
- the PBS utilisation of PrEP to date being lower than anticipated; and
- observed real-world reduction in new HIV notifications in the men-who-have-sex-with-men (MSM) population since 2014, including state-based demonstration programs and PBS listings.

6.3 The PBAC noted the price of PrEP had reduced by 58% (at the AEMP level) and the annual treatment cost with TD/FTC was approximately $1,350 per year. The PBAC noted that while the Kirby Institute model was of limited applicability to the revised population defined in the ASHM Guidelines; that within these limitations the cost-effectiveness of PrEP was below $30,000 per QALY in all model scenarios. The PBAC also recalled in its previous recommendation of PrEP that studies had indicated a proportion of patients had expressed an unwillingness to use PrEP and that individuals who self-identified as being at higher risk of acquiring HIV were likely to be more willing to use it. The Committee considered that while there were uncertainties in the cost-effectiveness of PrEP due to differences in the Kirby model and revised ASHM guidelines populations, the current price of PrEP provided additional confidence that

[7] Refers to a person whose sense of personal identity and gender corresponds with their birth sex.

PrEP was likely to be acceptably cost-effective in an expanded at-risk population that was not bound by the level of risk. The PBAC considered that, at the current price, PrEP use in the population defined in the revised ASHM Guidelines was likely to be cost-effective for those at-risk individuals who are most likely to seek treatment.

6.4 The Committee noted the real-world data referred to by the ASHM, such as the annual surveillance reports published by the Kirby Institute, showed a decline in new HIV notifications between 2014 – 2018, particularly in the MSM population; and this trend aligned with the period in which state-based PrEP demonstration projects commenced. The PBAC considered the ongoing surveillance data reinforced that the availability of subsidised PrEP likely had substantial impact for the MSM population and was effective at reducing the transmission of HIV in the real-world setting.

6.5 The PBAC noted the revised 2019 ASHM Guidelines removed reference to the level of patient risk based on past and present behaviour and now establish risk through identifying individual behaviours amongst different groups. The PBAC considered the revised criteria were more patient-centric and whilst they may increase demand for PrEP, it was unlikely the changed criteria and restriction type would lead to a substantial increase in PBS use.

6.6 In making a recommendation to change from a streamlined authority listing to a Restricted Benefit listing, the PBAC was satisfied that given the demonstrated impact of PrEP on HIV transmission in the MSM population, the current price of TD/FTC and likely further reductions due to price disclosure, that the use of PBS-subsidised PrEP could be supported for individuals who are likely to engage in risk behaviours and are willing to use PrEP. The PBAC considered the revised listing should not include specific criteria for risk or reference to specific guidelines and removal of the current age restrictions to allow for case-by-base decision-making between patients and clinicians. The Committee agreed the ASHM Guidelines provide a framework for such decision-making. The PBAC considered that the requirement for patients to have their HIV negative status confirmed between each 3-month supply of PrEP should remain to ensure patients who acquire HIV are managed appropriately and to provide opportunities for regular sexual health check-ups. The PBAC considered the wording should be flexible and not preclude treatment if the test result is not available at time of prescribing.

6.7 The PBAC noted the PBS utilisation of PrEP has increased in a broadly linear fashion since listing in April 2018 until late 2019, from about 5,000 monthly prescriptions in the initial months since listing to a plateau of about 18,000 per month (~12,000 discrete patients) from September 2019 onwards. The PBAC recalled it had considered the likely uptake of PrEP to be in the order of 60-70% of eligible individuals (based on the 2017 guidelines), or in a range of approximately 16,000-19,000 individuals in 2019. Based on the available data, the PBAC noted the use of PrEP in 2019 was lower than expected. However, PBAC considered the disparity between number of supplied prescriptions and number of patients warranted further review. The PBAC also considered the rate and level of price reductions for TD/FTC on the PBS contributed substantially to expenditure being lower than expected.

6.8 The Committee also noted the PBS use of PrEP declined about 50% compared to March 2020 and had partially recovered in subsequent months. The PBAC considered

the substantial changes in PrEP dispensing from April 2020 onwards were likely driven by individuals' behaviour changes attributable to COVID-19 and associated public health measures, such as restrictions on movement and gatherings.

6.9 The PBAC noted this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Amend existing listing as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TENOFOVIR with EMTRICITABINE tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet, 30	11276L	1	30	2	Tenofovir/Emtricitabine 300/200 APOTEX Apotex Pty Ltd
tenofovir disoproxil maleate 300 mg + emtricitabine 200 mg tablet, 30	11296M	1	30	2	Tenofovir Disoproxil Emtricitabine Mylan 300/200 Alphapharm Pty Ltd
tenofovir disoproxil phosphate 291 mg + emtricitabine 200 mg tablet, 30	11306C	1	30	2	Tenofovir EMT GH Generic Health Pty Ltd

Restriction Summary 7580 / ToC: 7580:

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
Restriction Type: ☒~~Authority Required – Streamlined [7580]~~ ☒*Restricted benefit*
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: Pharmaceutical benefits that have the forms tenofovir disoproxil phosphate 291 mg with emtricitabine 200 mg tablet, tenofovir disoproxil maleate 300 mg with emtricitabine 200 mg tablet, and tenofovir disoproxil fumarate 300 mg with emtricitabine 200 mg tablet are equivalent for the purposes of substitution.
Indication: Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection
~~**Clinical criteria:**~~
~~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~~
AND
Clinical criteria:
Patient must have-*at least one of the following prior to having the latest PBS-subsidised prescription issued: (i)* a negative HIV test result *no older than 4 weeks*, ~~prior to treatment with PBS-subsidised therapy with this drug~~ *(ii) evidence that a HIV test has been conducted, but the result is still forthcoming,* .
~~**Population criteria:**~~
~~Patient must be 18 years or older.~~

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.