PUBLIC SUMMARY DOCUMENT
Product: Tenofovir Disoproxil Fumarate, tablet 300 mg, Viread®
Sponsor: Gilead Sciences Pty Ltd
Date of PBAC Consideration: November 2008

1. Purpose of Application

The submission sought to extend the current Section 100 (Highly Specialised Drug) listing to include treatment of chronic hepatitis B (CHB).

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

2. Background

At its June 2002 meeting, the PBAC recommended listing of tenofovir under Section 100 for treatment in combination with other anti-retroviral drugs, of HIV infection in patients who have failed or experienced treatment-limiting toxicity with their current antiretroviral regimen and for whom a variable regimen cannot be constructed from other classes of anti-retroviral agents.

At its November 2004 meeting, the PBAC recommended extending the listing of tenofovir to that of other nucleoside reverse transcriptase inhibitors (NRTIs) listed on the PBS.

Tenofovir had not previously been considered by the PBAC for the treatment of CHB.

3. Registration Status

Tenofovir was first registered by the TGA on 13 August 2002 and is indicated for use in combination with other retroviral agents for the treatment of HIV-infected adults. Evidence to support this indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts in controlled studies of tenofovir in treatment-naïve adults and in treatment-experienced adults. In July 2008, the TGA approved indications were extended to include treatment of CHB in adults with evidence of active viral replication and active liver inflammation.

4. Listing Requested and PBAC's View

Section 100 – Highly Specialised Drugs Program
<u>Private hospital authority required.</u>
Treatment of HIV infection in patients with:

(a) CD4 cell counts of less than 500 per cubic millimetre; or
(b) Viral load of greater than 10,000 copies per mL.

Treatment-naïve chronic hepatitis B patients who satisfy all of the following criteria:

(1) Histological evidence of chronic hepatitis on liver biopsy (except in patient for whom a liver biopsy is contraindicated);
(2) Abnormal serum ALT levels and / or elevated HBV DNA in conjunction with documented chronic hepatitis B infection.

Chronic hepatitis B in patients who have failed antihepadnaviral therapy and who satisfy all of the following criteria:

(1) Repeatedly elevated serum ALT levels despite antihepadnaviral therapy of greater than or equal to 6 months duration with documented chronic hepatitis B infection or;
(2) Persistently elevated HBV DNA levels despite prior antihepadnaviral therapy of greater than or equal to 6 months duration or failure to achieve a 1 log reduction in HBV DNA within 3 months of commencing antihepadnaviral therapy except in patients with evidence of poor compliance.

NOTE:
Patients who have failed prior antihepadnaviral therapy may receive tenofovir treatment in combination with lamivudine.
Patients should have undergone a liver biopsy at some point since initial diagnosis to obtain histological evidence of chronic hepatitis.
Persons with Child's class B or C cirrhosis (ascites, variceal bleeding, encephalopathy, albumin less than 30 g per L, bilirubin greater than 30 micromoles per L) should have their treatment discussed with a transplant unit prior to initiating therapy.
Female patients who are of child-bearing age should not be pregnant, should not be breast-feeding, and should be using an effective form of contraception.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Tenofovir would provide an alternative oral treatment for chronic hepatitis B in both treatment naïve and treatment experienced patients.

6. Comparator

The submission nominated entecavir monohydrate 0.5 mg for nucleos(t)ide naïve patients, and adefovir dipivoxil 10 mg for nucleos(t)ide experienced patients. These were considered appropriate by PBAC.

7. Clinical Trials

Nucleos(t)ide naïve patients

The basis of the submission for tenofovir in nucleos(t)ide naïve patients was an adjusted indirect comparison[1] of one randomised trial of tenofovir 300 mg and one randomised trial of entecavir 0.5mg, with adefovir 10mg as the common reference, for hepatitis B e antigen (HBeAg) positive patients over 48 weeks; an unadjusted indirect comparison of the tenofovir 300mg arm of a randomised trial in HBeAg positive patients and the tenofovir 300mg arm of a randomised trial in HBeAg negative patients; and an unadjusted indirect comparison of the entecavir 0.5mg arm of a randomised trial in HBeAg positive patients and the entecavir 0.5mg arm of a randomised trial in HBeAg negative patients. Details of the studies published at the time of the submission are presented in the table below.

Trials and studies presented in the submission – nucleos(t)ide naïve patients

Trial ID/ Author	Protocol title/ Publication title	Publication citation
Indirect comparison in HBeAg positive patients – common reference adefovir		

[1] An adjusted indirect comparison is one in which the indirect comparison of intervention B and C is adjusted by the results of their direct comparisons with a common intervention. Song F, Altman D, *et al* Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ* 2003; 326: 472.

Tenofovir		
0103 HBeAg positive patients	GS-US-174-0103. A randomised double-blind, controlled evaluation of tenofovir DF versus adefovir dipivoxil for the treatment of HBeAg positive chronic hepatitis B.	Report date: August 2007 http://www.clinicaltrials.gov/ct2/show/NCT00116805?term=GS-US-174-0103&rank=1
Entecavir		
Leung 2007 HBeAg positive patients	Entecavir results in higher HBV DNA reduction versus adefovir in chronically infected HBeAg positive antiviral-naïve adults: 48 week results (EARLY study). Entecavir results in higher HBV DNA reduction vs. adefovir in chronically infected HBEAG (plus) antiviral-naïve adult: 24 wk results (EARLY study). Entecavir results in higher HBV DNA reduction versus adefovir in antiviral-naïve HBeAg(+) adults with high HBV DNA: week 96 results (EARLY study).	Leung, N *et al.* 42nd Annual Meeting of the European Association for the Study of the Liver (2007). Leung N, Peng C, Sollano J, Lesmana L, Yuen MF, Jeffers L, *et al*. *Hepatology* 2006; 44: 554A Leung N, Peng CY, Sollano J, Lesmana L, Yuen MF, Jeffers L, *et al.* 43rd Meeting of the European Association for the Study of the Liver (2008).
Naïve indirect comparison between HBeAg positive and HBeAg negative patients		
Tenofovir		
0102 HBeAg negative patients	GS-US-174-0102. A randomised, double-blind, controlled evaluation of tenofovir DF versus adefovir dipivoxil for the treatment of presumed pre-core mutant chronic hepatitis B.	Report date: August 2007 http://www.clinicaltrials.gov/ct2/results?term=GS-US-174-0102
0103 HBeAg positive patients	GS-US-174-0103. A randomised double-blind, controlled evaluation of tenofovir DF versus adefovir dipivoxil for the treatment of HBeAg positive chronic hepatitis B.	Report date: August 2007 http://www.clinicaltrials.gov/ct2/results?term=GS-US-174-0103
Entecavir		
Chang 2006 HBeAg positive patients	A comparison of entecavir and lamivudine for HBeAg positive chronic hepatitis B. Entecavir is superior to lamivudine for the treatment of HBeAg(+) chronic hepatitis B: results of phase III study ETV- 022 in nucleoside-naïve patients.	Chang T, Gish R, de Man R, Gadano A, Sollano J, Chao Y, *et al.* *New Engl J Med* 2006; 354: 1001–1010. Chang T, Gish R, de Man R, Gadano A, Sollano J, Han K, *et al. Hepatol* 2004; 40: 193A.
	Entecavir therapy for up to 96 weeks in patients with HBeAg positive chronic hepatitis B.	Gish R, Lok A, Chang T, de Man R, Gadano A, Sollano J, *et al.* *Gastroenterol* 2007; 133: 1437–1444

Lai 2006 HBeAg negative patients	Entecavir versus lamivudine for patients with HBeAg negative chronic hepatitis B.	Lai C, Shouval D, Lok A, Chang T, Cheinquer H, Goodman Z, *et al*. *New Engl Med* 2006; 354: 1011–1020.

DF=disoproxil fumarate; DNA= deoxyribonucleic acid; HBeAg and HBEAG=hepatitis B e antigen; HBV=hepatitis B virus; HIV=human immunodeficiency virus.

Nucleos(t)ide experienced patients

The basis of the submission for tenofovir in nucleos(t)ide experienced patients was a comparison of tenofovir 300mg and adefovir 10mg using the combined subgroups of experienced patients from two direct randomised trials, the first in HBeAg positive patients and the second in HBeAg negative patients. Conventional meta-analytic techniques were not used for this comparison. Supportive trials include one randomised trial comparing tenofovir monotherapy with tenofovir/emtricitabine combination therapy; an open label study of tenofovir/lamivudine combination therapy in patients with lamivudine resistance and suboptimal response to adefovir; one small randomised trial comparing tenofovir with adefovir in patients co-infected with human immunodeficiency virus (HIV) and hepatitis B virus (HBV); and one study comparing tenofovir/lamivudine combination therapy with lamivudine monotherapy in HIV/HBV co-infected patients. Details are presented in the table below.

Trials and studies presented in the submission – nucleos(t)ide experienced patients.

Trial ID/ Author	Protocol title / Publication title	Publication citation
0102 (subgroup) HBeAg negative patients combined with 0103 (subgroup) HBeAg positive patients	GS-US-174-0102. A randomised, double-blind, controlled evaluation of tenofovir DF versus adefovir dipivoxil for the treatment of presumed pre-core mutant chronic hepatitis B. GS-US-174-0103. A randomised double-blind, controlled evaluation of tenofovir DF versus adefovir dipivoxil for the treatment of HBeAg positive chronic hepatitis B.	Report date: August 2007 http://www.clinicaltrials.gov/ct2/results?term=GS-US-174-0102 Report date: August 2007 http://www.clinicaltrials.gov/ct2/results?term=GS-US-174-0103
0106 HBeAg positive patients and HBeAg negative patients	GS-US-174-0106. A phase 2, randomised, double-blind study exploring the efficacy, safety and tolerability of tenofovir disoproxil fumarate (DF) monotherapy versus emtricitabine plus tenofovir DF fixed-dose combination therapy in subjects currently being treated with adefovir dipivoxil for chronic hepatitis B and having persistent viral replication.	Report date: August 2007. http://www.clinicaltrials.gov/ct2/results?term=GS-US-174-0106

0109 HBeAg positive patients and HBeAg negative patients	IN-AU-174-0109. An open label study evaluating the antiviral activity of tenofovir DF 300mg daily in patients with chronic hepatitis B infection and persistent viral replication after long-term therapy with adefovir dipivoxil 10mg daily. A prospective study of tenofovir disoproxil fumarate for patients with chronic hepatitis B who have previously failed lamivudine and have persistent viral replication despite at least 24 weeks of adefovir therapy.	Protocol date: 10 May 2006. Patterson S, Lee A, Strasser S, Desmond P, Roberts S, Angus P, *et al*. Unpublished.
Dore 2004 (substudy 903) HBeAg positive patients and HBeAg negative patients	Efficacy of tenofovir disoproxil fumarate in antiretroviral therapy-naïve and –experienced patients co-infected with HIV-1 and hepatitis B virus.	Dore G, Cooper D, Pozniak A, DeJesus E, Zhong L, Miller M, *et al. J Infect Dis* 2004; 189: 1185–1192.
Peters 2006 HBeAg positive patients and HBeAg negative patients	Randomised controlled study of tenofovir and adefovir in chronic hepatitis B virus and HIV infection: ACTG A5127.	Peters M, Andersen J, Lynch P, Liu T, Alston-Smith B, Brosgart C, *et al*, for the ACTG Protocol A5127 Team. *Hepatol* 2006; 44: 1110–1116.

ACTG=Adult AIDS Clinical Trials Group; DF=disoproxil fumarate; DNA= deoxyribonucleic acid; HBeAg=hepatitis B e antigen; HBV=hepatitis B virus; HIV=human immunodeficiency virus.

8. Results of Trials

1) Nucleos(t)ide naïve patients

The submission aimed to demonstrate the non-inferiority of tenofovir 300mg to entecavir 0.5mg. The submission argued that the following chain of logic leads to the conclusion that tenofovir is non-inferior to entecavir 0.5mg in both HBeAg positive and HBeAg negative patients:

1. Tenofovir is non-inferior to entecavir 0.5mg in HBeAg positive CHB patients. The evidence presented was an adjusted indirect comparison of tenofovir and entecavir from one randomised trial of tenofovir in HBeAg positive patients (0103) and one randomised trial of entecavir 0.5mg in HBeAg positive patients (Leung 2007). The common reference for this indirect comparison was adefovir.

Summary of results of the indirect comparison of tenofovir versus entecavir in nucleos(t)ide-naïve, HBeAg positive patients

	0103			Leung 2007			Adjusted indirect estimate of effect (95%CI)
HBV <300 copies/ mL	Treatment effect[a] (95% CI)	Tenofovir n/N (%)	ADV n/N (%)	ADV n/N (%)	Entecavir n/N (%)	Treatment effect[b] (95% CI)	

Relative risk	6.04 (3.45,10.6)	130/176 (74)	11/90 (12)	6/32 (19)	19/33 (58)	3.07 (1.41,6.69)	1.97 (0.75,5.14)
***Odds ratio*[c]**	*20.30 (9.93,41.5)*					*5.88 (1.91,18.1)*	*3.45 (0.91,13.1)*

ADV=adefovir; CI, confidence interval; n, number of participants reporting data; N, total participants in group, RR, relative risk
[a] Tenofovir over adefovir
[b] Entecavir over adefovir
[c] *Calculated during the evaluation*

The submission stated that no significant difference was detected between patients treated with tenofovir (74%) and patients treated with entecavir (58%). A non-inferiority margin was not specified. The width of the adjusted confidence interval strongly suggested that this comparison was underpowered.

Due to the lack of a study allowing a common comparator the following logic was applied for comparison to entecavir in HBeAg negative CHB.

2. Tenofovir has similar efficacy in both HBeAg positive and HBeAg negative CHB patients. The basis of this argument was an unadjusted comparison of the tenofovir treatment arms from trials 0102 and 0103 without use of a common reference.

3. Entecavir has similar efficacy in both HBeAg positive and HBeAg negative CHB patients. The basis of this argument was an unadjusted comparison of the entecavir treatment arms from trials Chang 2006 and Lai 2006 without use of a common reference.

4. From points 2-3, it is claimed that tenofovir is also non-inferior to entecavir in HBeAg negative CHB patients.

The results of the unadjusted indirect comparison that were intended to demonstrate equivalent efficacy of firstly tenofovir (point 2 above), and secondly entecavir (point 3 above), in HBeAg positive versus HBeAg negative patients are presented in the following tables.

Summary of the main results of the unadjusted indirect comparison without a common reference of tenofovir in HBeAg positive patients versus HBeAg negative patients-nucleos(t)ide naive

	0102 HBeAg negative	**0103 HBeAg positive**		
Outcome	**Tenofovir *n*/*N* (%)**	**Tenofovir *n*/*N* (%)**	***OR*[a] *(95% CI)***	**p-value[b]**
Complete response	177/250 (70.8)	117/176 (66.5)	*1.22 (0.81, 1.85)*	0.34
HBV DNA <300 Copies/mL	236/250 (92.0)	130/176 (73.9)	*5.28 (2.78, 10.03)*	<0.001

CI = confidence interval; *n* = number with event; *N* = number in group; OR = odds ratio
[a] *Calculated during the evaluation*
[b] Comparison of tenofovir HBeAg positive and tenofovir HBeAg negative
Underlined text indicates primary outcome measure

Summary of the main results of the unadjusted indirect comparison without a common reference of entecavir in HBeAg positive patients versus HBeAg negative patients – nucleos(t)ide naïve patients.

	Lai 2006 HBeAg negative	Chang 2006 HBeAg positive		
Outcome	**Entecavir *n*/*N* (%)**	**Entecavir *n*/*N* (%)**	***OR*[a] *(95% CI)***	**p-value[b]**
Histologic response	208/296 (70)	226/314 (72)	*0.92* *(0.65, 1.31)*	0.64
HBV DNA <300 copies/mL	293/325 (90)	236/354 (67)	*4.58* *(2.99, 7.01)*	<0.001

CI=confidence interval; LMV=lamivudine *n* = number with event; *N* = number in group; OR=odds ratio
[a] *Calculated during the evaluation*
[b] Comparison of entecavir HBeAg positive and entecavir HBeAg negative
Underlined text indicates primary outcome measure

The claim that tenofovir is equally effective in HBeAg negative and HBeAg positive patients, and the similar claim for entecavir, were based on the p-values for the respective primary outcomes of each of the unadjusted indirect comparisons, and no statistically significant difference between the relevant patient groups for the primary outcomes of the different trials.

For PBAC's comments on these results, see Recommendation and Reasons.

2) Nucleos(t)ide experienced patients

The submission aimed to demonstrate non-inferiority of tenofovir 300mg to adefovir 10mg.

The key evidence presented to support the requested listing of tenofovir for treatment of CHB in nucleos(t)ide experienced patients was a direct comparison of tenofovir and adefovir using the combined results for the subgroups of experienced patients from single arms of two randomised controlled trials (RCTs), one in HBeAg positive patients and one in HBeAg negative patients.

Summary of results of the direct comparison of tenofovir versus adefovir in nucleos(t)ide-experienced patients (combined analysis from studies 0102 and 0103)

Outcome	**Tenofovir n/N (%)**	**Adefovir n/N (%)**	***RR*[a] *(95% CI)***	***OR*[a] *(95% CI)***	**p-value**
Complete response	37/51 (72.5)	15/24 (62.5)	*1.16* *(0.82, 1.65)*	*1.59* *(0.57, 4.44)*	0.390
HBV DNA <400 copies/mL	46/51 (90.2)	17/24 (70.8)	*1.27* *(0.9, 1.67)*	*3.79* *(1.06,13.56)*	0.057 *(0.068)*
Histologic response	40/51 (78.4)	21/24 (87.5)	*0.90* *(0.73, 1.10)*	*0.52* *(0.13, 2.07)*	0.307

CI=confidence interval; DNA=deoxyribonucleic acid; HBV=hepatitis B virus; *n* = number with event; *N* = number in group; OR=odds ratio
[a] *Calculated during the evaluation*

For PBAC's comments on these results, see Recommendation and Reasons.

Direct comparative safety data on tenofovir versus entecavir in nucleos(t)ide naïve patients were not presented in the submission. The majority of the comparative safety data for tenofovir versus adefovir was from the two key RCTs in predominantly treatment naïve patients. The PBAC noted that overall, the frequencies of adverse events were similar for tenofovir and adefovir, with the exception of nausea, which occurred more often in the tenofovir treatment group. The most frequently occurring adverse events were headache, nasopharyngitis, and back pain. Grade 3 or 4 adverse events, serious adverse events and adverse events resulting in permanent discontinuation or interruption of study drug were all infrequent and occurred at similar rates in both groups. No adverse event led to discontinuation in more than one subject. The safety profile of tenofovir in CHB patients was consistent with the known safety profile of tenofovir in patient with HIV infection.

9. Clinical Claim

The submission described tenofovir as non-inferior in terms of comparative effectiveness and non-inferior in terms of comparative safety to entecavir 0.5mg in nucleos(t)ide naïve patients, and to adefovir in nucleos(t)ide experienced patients.

The PBAC accepted the claim of non-inferiority of tenofovir to entecavir 0.5 mg in HBeAg positive CHB nucleoside naïve patients. Based on the data provided, the Committee did not accept the claim that tenofovir is equally effective in nucleoside naïve HBeAg negative and HBeAg positive patients, or the similar claim for entecavir.

10. Economic Analysis

The submission presented a cost minimisation analysis. The equi-effective doses of tenofovir 300 mg per day and entecavir 0.5 mg per day were accepted by the PBAC for the treatment of HBeAg positive nucleoside naïve patients. Because non-inferiority had not been established beyond reasonable doubt (see above), the claim of equi-effectiveness at these doses for the other requested listings is not supportable.

11. Estimated PBS Usage and Financial Implications

The submission estimated the likely number of patients per year to be less than 10,000 in Year 5. The PBAC considered that the estimate was likely an overestimate.

The submission estimated financial savings per year to the PBS of less than $10 million in Year 5. The submission's estimate is a combined cost for nucleos(t)ide naïve and experienced patients.

The submission estimated the financial cost per year to the PBS in nucleos(t)ide naïve patients to be less than $10 million in Year 5.

The submission estimated the financial savings per year to the PBS in nucleos(t)ide experienced patients at less than $10 million in Year 5.

12. Recommendation and Reasons

The PBAC recommended the listing of tenofovir on the S100 Highly Specialised Drugs Program of the PBS for the treatment patients with HBeAg-positive chronic hepatitis B (CHB) who are nucleoside analogue naïve on a cost minimisation basis to entecavir 0.5 mg tablets. The equi-effective doses in this indication are tenofovir 300 mg per day and entecavir 0.5 mg per day. The Committee also recommended that a new total expenditure

cap should be developed for tenofovir to manage the possibility of use outside the PBS indication.

In making this recommendation the Committee agreed that the comparators entecavir monohydrate 0.5 mg for patients naïve to nucleos(t)ide therapy and adefovir dipivoxil 10 mg for patients who have failed previous nucleos(t)ide therapy were appropriate.

The PBAC further accepted the claim of non-inferiority of tenofovir to entecavir 0.5 mg in HBeAg positive CHB nucleoside naïve patients based on the adjusted indirect comparison of tenofovir to entecavir presented in the submission from the randomised trial of tenofovir in HBeAg positive patients (0103) to the randomised trial of entecavir 0.5 mg in HBeAg positive patients (Leung 2007) with the common reference of adefovir. Although a pre-defined non-inferiority threshold was not specified for the comparison, the Committee accepted the non-inferiority margin of 10 – 15 % proposed in the pre-Sub-Committee response.

The Committee did not accept, based on the data provided, the claim that tenofovir is equally effective in nucleoside naïve HBeAg negative patients to entecavir because this conclusion relies on the assumption that tenofovir is equally effective in nucleoside naïve HBeAg negative and HBeAg positive patients, and considered the unadjusted comparison of the tenofovir treatment arms from trials 0102 in HBeAg negative patients and 0103 in HBeAg positive patients without use of a common reference, to represent insufficient evidence. The PBAC considered that HBeAg positive CHB and HBeAg negative CHB are well established as being distinct disease entities and that HBeAg status is both an effect modifier and an independent predictor of outcome. Further, a comparison of outcomes between HBeAg positive patients from one study and HBeAg negative patients from another study is subject to considerable confounding with important differences between the baseline characteristics of the patients in the trials, in addition to HBeAg status, that may influence the outcome. The PBAC did not accept the claim that the lack of a statistically significant difference between HBeAg positive and HBeAg negative subgroups from the different trials for the primary outcome is evidence that the treatment is equally effective in the two groups. The Committee hence rejected the application for listing of tenofovir in HBeAg negative nucleoside naïve CHB patients, considering insufficient evidence had been presented to support the claim of non-inferiority to entecavir 0.5 mg.

In nucleoside treatment experienced patients the PBAC again considered the methods used in the submission for the direct comparison of tenofovir to adefovir, in which the results of the subgroups of nucleoside experienced patients from a trial in HBeAg positive CHB patients and a trial in HBeAg negative CHB patients were combined, to be flawed. The Committee also noted that non-inferiority margins were not pre-specified for the subgroup analysis, and that using the non-inferiority margins specified in the original studies, the subgroup analysis does not support the claim that tenofovir is non-inferior to adefovir in treatment-experienced patients. The Committee hence rejected the application for listing of tenofovir for the treatment of CHB in nucleoside experienced patients.

Recommendation

TENOFOVIR DISOPROXIL FUMARATE, tablet, 300 mg

Restriction: Section 100 – Highly Specialised Drugs Program

Private hospital authority required
Treatment of HIV infection in patients with:

(a) CD4 cell counts of less than 500 per cubic millimetre; or
(b) Viral load of greater than 10,000 copies per mL.

Treatment, as sole PBS-subsidised therapy, in a patient with HBeAg-positive chronic hepatitis B who is nucleoside analogue naive and satisfies all of the following criteria:
(1) Histological evidence of chronic hepatitis on liver biopsy (except in patients with coagulation disorders considered severe enough to prevent liver biopsy);
(2)(a) Abnormal serum ALT levels in conjunction with documented chronic hepatitis B infection; or
(b) Elevated HBV DNA levels in conjunction with documented chronic hepatitis B infection;
(3) Female patients of child-bearing age are not pregnant, not breast-feeding, and are using an effective form of contraception.
Persons with Child's class B or C cirrhosis (ascites, variceal bleeding, encephalopathy, albumin less than 30 g per L, bilirubin greater than 30 micromoles per L) should have their treatment discussed with a transplant unit prior to initiating therapy.

Pack size: 30

13. 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.

14. Sponsor's Comment

The sponsor welcomes the recommendation by the PBAC for the PBS listing of tenofovir for treatment naïve patients with HBeAg positive chronic Hepatitis B. The sponsor is committed to continue to work closely with the PBAC and will address areas of uncertainty that remain in order to obtain a recommendation for HBeAg negative and treatment experienced patients.