PUBLIC SUMMARY DOCUMENT
Product: Telaprevir, tablet, 375 mg, Incivo®
Sponsor: Janssen-Cilag Pty Ltd
Date of PBAC Consideration: March 2012

1. Purpose of Application

The submission sought Section 100 (Highly Specialised Drugs Program) Private Hospital Authority Required and Public Hospital Authority Required (STREAMLINED) listings for the treatment, in combination with peginterferon-alfa and ribavirin, of chronic genotype 1 hepatitis C in a patient 18 years or older who has compensated liver disease and meets certain criteria.

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

This was the second submission for telaprevir considered by the PBAC.

At its November 2011 meeting, the PBAC rejected an application seeking listing of telaprevir for treatment in combination with peginterferon-alfa and ribavirin of patients aged 18 years or older with chronic hepatitis C who have failed to respond to prior interferon based therapies (treatment experienced patients) on the basis of uncertainty about the impact of the final product information resulting from the evaluation by the Therapeutics Goods Administration (TGA) on all aspects of the submission with resultant uncertain cost effectiveness and highly uncertain utilisation.

The application to the November 2011 PBAC meeting was made under TGA/PBAC parallel process provisions. No TGA documentation was available at the time of PBAC consideration in November 2011.

A copy of the Public Summary Document from the November 2011 meeting is available at http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-telaprevir-nov11

3. Registration Status

Telaprevir was TGA registered on 6 March 2012 for the following indication:

Telaprevir, in combination with peginterferon alfa and ribavirin, is indicated for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease (including cirrhosis):
- who are treatment naïve;
- who have previously been treated with interferon alfa (pegylated or non pegylated) alone or in combination with ribavirin, including relapsers, partial responders and null responders.

4. Listing Requested and PBAC's View

Section 100 (Highly Specialised Drugs Program)
Private Hospital Authority Required

Public Hospital Authority Required (STREAMLINED)
Treatment of telaprevir in combination with peginterferon-alfa and ribavirin, managed by an accredited treatment centre, of chronic hepatitis C in patients 18 years or older who have compensated liver disease and who satisfy all of the following criteria:

(1) Documented chronic genotype 1 hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive);
(2) Female patients of child-bearing age who are not pregnant, not breast-feeding, and both patient and their partner are using effective forms of contraception (one for each partner). Female partners of male patients are not pregnant.

The treatment course is limited to one course of 12 weeks. Patients may only continue treatment after the first 6 weeks if the results of a HCV RNA quantitative assay at Week 4 (performed at the same laboratory using the same test) shows that the plasma HCV RNA has become ≤ 1,000 IU/mL.

Note
Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:

(a) nurse / educator / counsellor for patients; and
(b) 24 hour access by patients to medical advice; and
(c) An established liver clinic; and
(d) Facilities for safe liver biopsy.

The PBAC noted that the March 2012 submission presented data in treatment naïve patients (*see Clinical Trials*) and that the previous November 2011 submission presented data in treatment experienced patients and so the March 2012 submission requested listing in both patient groups and included data from both the treatment naive and treatment experienced populations in an economic model.

The PBAC had previously considered that the restriction should exclude use of telaprevir in patients who have failed to respond to other HCV N3S 4A protease inhibitors. Additionally, the PBAC considered that telaprevir meets the conditions for listing as a Section 100 Highly Specialised Drug. *See Recommendation and Reasons.*

5. Clinical Place for the Proposed Therapy

Chronic hepatitis C virus infection is a slow progressing disease that can lead to cirrhosis of the liver, hepatocellular carcinoma and eventually death. There are several hepatitis C virus genotypes, the most common being genotypes 1, 2 and 3 in Australia. Patients with genotype 1 hepatitis C make up the majority (55%) of cases in Australia, and are the least responsive to standard therapy (peginterferon with ribavirin) despite prolonged treatment.

The submission proposed that telaprevir in combination with peginterferon alfa with ribavirin would provide an additional treatment option for patients with chronic hepatitis C genotype 1.

6. Comparator

The submission nominated peginterferon alfa and ribavirin (PR), without a concomitant direct acting antiviral agent, as the comparator for telaprevir administered in combination

with PR. The PBAC considered the comparator of peginterferon alfa and ribavirin alone for a duration of 48 weeks was appropriate.

The submission also nominated boceprevir, in combination with PR, as a minor comparator, in anticipation that boceprevir is likely to be registered for use in Australia at a similar time to telaprevir.

7. Clinical Trials

The primary evidence presented in the submission was one three-armed direct randomised trial comparing two regimens of telaprevir therapy (8 weeks and 12 weeks), both given in combination with either 24 weeks or 48 weeks of peginterferon alfa 2a and ribavirin (depending on the patient's virological response), with 12 weeks of placebo in combination with 48 weeks of peginterferon alfa 2a and ribavirin, in treatment naïve genotype 1 chronic hepatitis C (CHC) patients (ADVANCE).

Supplementary evidence presented in the submission included:

- Two supplementary four-armed direct randomised trials comparing either 8 or 12 weeks of telaprevir therapy, in combination with varying durations of peginterferon alfa 2a (12, 24 or 48 weeks) with or without ribavirin, with placebo in combination with 48 weeks of peginterferon alfa 2a and ribavirin, in treatment naïve genotype 1 CHC patients (PROVE 1 and PROVE 2);
- One supplementary direct randomised trial comparing 12 weeks of telaprevir therapy, in combination with peginterferon alfa 2b plus ribavirin, with 48 weeks of peginterferon alfa 2b and ribavirin (Kumada 2011); and
- One supplementary two-armed randomised trial comparing 12 weeks of telaprevir therapy, in combination with 24 weeks of peginterferon alfa 2a and ribavirin, with 12 weeks of telaprevir therapy in combination with 48 weeks of peginterferon alfa 2a and ribavirin, in treatment naïve genotype 1 CHC patients who achieve an extended rapid virological response (eRVR) (ILLUMINATE). This trial was not placebo-controlled but was presented to justify the shorter duration of PR therapy in non-cirrhotic patients who achieve an eRVR.

Details of the trials published at the time of submission are shown below.

Trials and associated reports presented in the submission

Trial ID / First author	Protocol title/ Publication title	Publication citation
1. Telaprevir/PR vs placebo/PR in treatment naïve patients		
Primary basis of submission		
ADVANCE Jacobson IM, et al.	Telaprevir for previously untreated chronic hepatitis C virus infection.	*New England Journal of Medicine* 2011; 364 (25):2405-2416.
Supplementary randomised trials		
PROVE 1 McHutchison JG, et al.	Telaprevir with peginterferon and ribavirin for chronic HCV genotype 1 infection.	*New England Journal of Medicine* 2009; 360 (18):1827-1838.
PROVE 2		

Hezode C, et al.	Telaprevir and peginterferon with or without ribavirin for chronic HCV infection.	*New England Journal of Medicine* 2009; 360 (18):1839-1850.
Kumada H, et al. (Study 6060-A6)	Telaprevir with peginterferon and ribavirin for treatment-naïve patients chronically infected with HCV of genotype 1 in Japan.	*Journal of Hepatology* 2011; doi:10.1016/j.hep.2011.07.016.
2. Telaprevir/PR24 vs telaprevir/PR48 in treatment naïve patients with eRVR		
Direct randomised trial		
ILLUMINATE Sherman KE, et al.	Response-guided telaprevir combination treatment for hepatitis C virus infection.	*New England Journal of Medicine* 2011; 365 (11):1014-24.

HCV = hepatitis C virus

The PBAC noted that the continuation criteria applied in the comparator arm of ADVANCE, PROVE 1 and 2 and Kumada et al. (2011) differed both from each other and from the continuation criteria in the existing PBS listing for peginterferon alfa and ribavirin for this patient group. Therefore, the comparator arms in the trials were not entirely consistent with current Australian standard of care. In addition, the treatment stopping rules applied in the telaprevir-containing arms of these trials were not consistent with the treatment continuation criteria proposed in the draft Product Information document included in the submission. The PBAC considered that this had implications for the applicability of the trial results to the Australian clinical setting.

8. Results of Trials

The primary outcome in both ADVANCE and ILLUMINATE was $SVR24_{planned}$, defined as undetectable HCV RNA levels 24 weeks after the last planned dose of study drug, known as a sustained virological response (SVR).

The following table presents the results for the primary outcome in the ADVANCE trial.

Results for the primary outcome, $SVR24_{planned}$, in ADVANCE

	T12PR24/48 n/N (%)	Pbo12/PR48 n/N (%)	Absolute risk difference % (95% CI)	Relative Risk (95% CI)	Odds Ratio (95% CI)
$SVR24_{planned}$					
FAS	271/363 (74.7)	158/361 (43.8)	30.9 (24.1, 37.7)	1.71 (1.50, 1.95)	3.95 (2.87, 5.45)
eRVR status					
eRVR +ve	189/212 (89.2)	-	-	-	-
eRVR -ve	82/151 (54.3)	-	-	-	-

CI = confidence interval; eRVR = extended rapid virological response; FAS = full analysis set; Pbo = placebo; PR = peginterferon alfa and ribavirin; SVR = sustained virological response; T = telaprevir

The PBAC noted that telaprevir administered in combination with PR (with the duration of PR treatment determined by virological response to treatment) significantly increased the proportion of treatment naïve genotype 1 CHC patients achieving $SVR24_{planned}$ in comparison to placebo in combination with a 48 week duration of PR in the ADVANCE trial.

The supplementary trials support the superiority of telaprevir+PR over placebo+PR as demonstrated by ADVANCE.

The results of the primary outcome in the ILLUMINATE trial, for both the full analysis set (FAS) and categorised by cirrhosis status, are presented below.

Results for the primary outcome, $SVR24_{planned}$, in ILLUMINATE – T12/PR24 versus T12/PR48 in patients achieving an eRVR

Outcome	T12PR24/ eRVR+ n/N (%)	T12PR48/ eRVR+ n/N (%)	Absolute risk difference[a] % (95% CI)	Relative Risk (95% CI)	Odds Ratio (95% CI)
$SVR24_{planned}$					
FAS[a]	149/162 (92.0)	140/160 (87.5)	4.5 (-2.1, 11.1)	1.05 (0.98,1.13)	1.62 (0.77, 3.38)
Cirrhosis[b]	12/18 (66.7)	11/12 (91.7)	-25.0 (-51.8, 1.81)	0.73 (0.50, 1.05)	0.18 (0.02, 1.76)
No cirrhosis	137/144 (95.1)	129/148 (87.2)	8.0 (1.5, 14.4)	1.09 (1.02, 1.17)	2.88 (1.17, 7.09)
Sensitivity analysis[c]	149/161 (92.5)	140/147 (95.2)	-2.7 (-8.0, 2.6)	0.97 (0.92, 1.03)	0.62 (0.24, 1.58)

CI = confidence interval; eRVR = extended rapid virological response; FAS = full analysis set; Pbo = placebo; PR = peginterferon alfa and ribavirin; SVR = sustained virological response; T = telaprevir

[a] The pre-specified non-inferiority margin was an absolute difference of 10.5%

[b] This is a post hoc analysis. Randomisation was not stratified by baseline cirrhosis status.

[c] Sensitivity analysis performed during the evaluation, excluding patients who discontinued treatment prior to commencement of the randomised treatment phase. These patients are assumed to have failed treatment.

There was considerable discrepancy between the two randomised groups in the number of patients discontinuing study drugs after Week 12 and prior to Week 24 (1/162, 0.6%, in the T12/PR24 arm compared to 13/160, 8.1%, in the T12/PR48 arm), despite the fact that both groups received the same treatment up to Week 24. As patients who discontinued treatment before Week 24 were less likely to achieve a sustained virological response (SVR), this imbalance probably favoured the T12/PR24 treatment regimen.

The result for the primary outcome, $SVR24_{planned}$, met the predefined non-inferiority criterion of an absolute difference of no more than 10.5%, when the analysis was conducted either on the full analysis set or on a per protocol basis. While the proportion of patients with $SVR24_{planned}$ categorised by liver disease status was a pre-specified outcome, the subgroup analysis of the comparative treatment effect in patients with cirrhosis was post hoc and was insufficiently powered to draw any conclusions regarding the relative effectiveness of the two telaprevir+PR regimens in this subgroup of patients.

For PBAC's view of these results, see Recommendations and Reasons.

The adverse events (AEs) during the telaprevir/placebo and overall treatment phases of the ADVANCE trial are summarised below.

Summary of adverse events in the ADVANCE trial

	T12PR24/48 n (%)	Pbo12/PR48 n (%)	Absolute risk difference (95% CI)
Telaprevir/placebo treatment phase (first 12 weeks)			
	(N = 363)	**(N = 361)**	
Any AE	361 (99.4)	347 (96.1)	
Any treatment-related AE	359 (98.9)	343 (95.0)	
Serious AE	19 (5.2)	7 (1.9)	
AE leading to death	0	0	
AE leading to reduction of dose of any study drug	126 (34.7)	82 (22.7)	12.0 (5.5, 18.5)
AE leading to interruption of dose of any study drug	50 (13.8)	20 (5.5)	8.2 (4.0, 12.5)
AE leading to permanent discontinuation of telaprevir/placebo	41 (11.3)	3 (0.8)	10.5 (7.1, 13.9)
AE leading to discontinuation of treatment regimen[a]	25 (6.9)	13 (3.6)	3.3 (0.0, 6.5)
Grade 3/4 AE	82 (22.6)	41 (11.4)	11.2 (5.8, 16.6)
Overall treatment phase (Week 1 to 24 or 48)			
Any AE	361 (99.4)	354 (98.1)	
Serious AE	33 (9.1)	24 (6.6)	
AE leading to death	0	1 (0.3)	
AE leading to reduction of dose of any study drug	165 (45.5)	116 (32.1)	13.3 (6.3, 20.4)
AE leading to interruption of dose of any study drug	59 (16.3)	36 (10.0)	6.3 (1.4, 11.2)
AE leading to discontinuation of treatment regimen	36 (9.9)	26 (7.2)	2.7 (-1.4, 6.8)
Grade 3/4 AE	103 (28.4)	68 (18.8)	9.5 (3.4, 15.7)

AE = adverse event; CI = confidence interval; Pbo = placebo; PR = peginterferon alfa and ribavirin; T = telaprevir

[a] Discontinuation of all study drugs (discontinuation of each study drug may not have occurred at the same time)

The submission stated that during the telaprevir/placebo treatment phase there was a significant increase in grade 3-4 AEs and AEs that led to dose reduction or interruption of any study drug in the telaprevir+PR groups compared to the placebo+PR group. These differences were also evident over the entire treatment phase.

Pruritus, rash, anaemia, dysgeusia (distortion of taste sensation) and gastrointestinal disorders (nausea, diarrhoea, vomiting, anorectal discomfort and dry mouth) occurred more frequently in the T12PR24/48 treatment arm compared to the Pbo12/PR48 arm.

Rash/pruritus was reported in approximately 55% of patients treated with telaprevir compared with approximately 34% of placebo+PR recipients. The majority of rash and pruritus events were mild to moderate in severity. In ADVANCE, more patients treated with telaprevir had grade 3 rash events (6.5% versus 0.6%) and rash events leading to discontinuation of telaprevir/placebo (6.6% versus 0.6%) compared to those treated with Pbo12/PR48.

In the ADVANCE trial, patients receiving telaprevir had a higher frequency of anaemia (36% versus 17.5%), serious events of anaemia (1.9% versus 0%), grade 3 anaemia (6.6%

versus 0.6%) and anaemia that led to the discontinuation of telaprevir/placebo (3.6% versus 0%) compared to patients in the Pbo12/PR48 arm. The majority of anaemia AEs were managed by dose reduction of at least one study drug (ribavirin). Five patients (1.4%) in the T12PR24/48 group and four (1.1%) in the Pbo12/PR48 group received erythropoietin (EPO) for the treatment of anaemia. 17 patients (4.7%) in the T12PR24/48 group and 6 (1.7%) in the Pbo12/PR48 group received a blood transfusion.

For PBAC's view, see Recommendation and Reasons.

9. Clinical Claim

The submission described telaprevir in combination with PR as superior in terms of comparative effectiveness over PR alone. The submission acknowledged that telaprevir in combination with PR is inferior in terms of comparative safety to PR alone during the 12 week telaprevir treatment phase, but argued that, across the entire course of therapy the comparative safety trends towards being non-inferior. The submission also claimed that treatment naïve patients who achieve an eRVR during treatment with telaprevir and PR can shorten their duration of PR treatment from 48 weeks to 24 weeks without any reduction in efficacy and with an improved safety profile.

The evidence presented supported the claim that telaprevir in combination with PR is superior to placebo in combination with PR therapy, in terms of sustained viral response 24 weeks after completion of the study drug regimen in genotype 1 CHC patients who have received no prior interferon based therapy.

The results of the ILLUMINATE trial supported the claim that, in treatment naïve patients achieving an eRVR, telaprevir in combination with a shortened duration of PR therapy (24 weeks) is non-inferior to telaprevir in combination with 48 weeks of PR therapy. As the post hoc analysis of patients with cirrhosis was insufficiently powered, the optimal duration of PR treatment in this subgroup was unclear.

The PBAC did not accept the claim of similar comparative safety of telaprevir+PR to PR across the full course of treatment.

For PBAC's view, see Recommendation and Reasons.

10. Economic Analysis

The submission presented a stepped economic evaluation of the use of telaprevir in the treatment naive setting, based on direct randomised trials. The type of economic evaluation presented was a cost-utility analysis. Another economic model was presented in which patients who received PR alone in the treatment naive setting and failed to achieve an SVR received telaprevir + PR in the treatment experienced setting.

The treatment naive economic evaluation had two components. The first was the short term (1 year) decision analytic model after which patients are deemed to have achieved SVR or not and are entered into the long term Markov model. Patients entered the model at 47 years of age. Patients were stratified by baseline liver disease (Mild HCV, Moderate HCV and Cirrhosis). The SVR rates were calculated for these subgroups and progression through the Markov model was determined by baseline liver disease. Patients with mild or moderate HCV who achieved an SVR remained at their baseline

liver disease until death. Patients who were cirrhotic and achieved an SVR had a small chance of developing hepatocellular carcinoma.

Patients who did not achieve SVR could have progressed through the following health states:

- Mild HCV
- Moderate HCV
- Cirrhosis
- Decompensated cirrhosis
- HCC
- Liver transplant (Year 1)
- Liver transplant (Year 2+)

A tunnel state following liver transplant was employed to capture the added risk of death in the first year following surgery.

All transition probabilities in the model remained constant, with the exception of death from all causes, which was sourced from Australian life tables.

In the treatment naive model, patients who did not achieve an SVR were not re-treated in the treatment experienced setting. However, another economic model was presented to analyse this scenario.

A lifetime (up to 60 years) time horizon was modelled.

Re-infection was not originally included in the model. However, as suggested by the PBAC for the telaprevir submission for treatment experienced CHC patients, the possibility of re-infection among patients who achieve a SVR should have been included in the economic evaluation. Additional analyses of reinfection and the treatment of anaemia were subsequently provided in the sponsor's pre-sub-committee response.

The base case incremental cost per extra QALY gained was between $15,000 and $45,000.

For PBAC's view, see Recommendation and Reasons.

11. Estimated PBS Usage and Financial Implications

The submission estimated the total net cost to the PBS of telaprevir to be between $30 – 60 million in Year 5 of listing, based on the assumption that boceprevir is listed on the PBS at a similar time.

The PBAC considered the utilisation estimates and hence the estimated financial cost to the PBS were highly uncertain.

For PBAC's view, see Recommendation and Reasons.

12. Recommendation and Reasons

The PBAC noted that telaprevir was now registered by the TGA and that the number of quantitative and qualitative HCV RNA assays in the dosing schedule in the approved Product Information and requested PBS listing were within the maximum number per

year currently subsidised under the Medical Benefits Schedule.

The PBAC considered the comparator of peginterferon alfa and ribavirin alone for a duration of 48 weeks was appropriate.

The PBAC noted that telaprevir administered in combination with PR (with the duration of PR treatment determined by virological response to treatment) significantly increased the proportion of treatment naïve genotype 1 chronic hepatitis C patients achieving the surrogate outcome of undetectable HCV RNA levels 24 weeks after the last planned dose of study drug in comparison to placebo in combination with a 48 week duration of PR in the ADVANCE trial. The PBAC also noted that the supplementary trials presented in the submission (PROVE 1, PROVE 2, Kumada 2011 and ILLUMINATE) supported the claim of superiority of telaprevir in combination with PR (telaprevir+PR) over placebo with PR in treatment naive genotype 1 chronic hepatitis C with the proposed treatment regimen in terms of sustained virological response.

The PBAC did not accept the claim of similar comparative safety of telaprevir+PR to PR across the full course of treatment. Based on the evidence presented, the PBAC considered telaprevir+PR is of inferior safety to PR alone, noting that there was an increase in adverse events with telaprevir+PR compared to PR alone across the overall treatment phase (week 1 to 24 or 48) in ADVANCE. The PBAC further noted that the most common treatment related serious adverse events with telaprevir+PR in comparison to PR alone were anaemia and skin disorders, such as rash.

The PBAC considered there were a number of uncertainties in the economic model, as identified by the Economics Sub-Committee including:

- A life time horizon of 60 years was modelled. The PBAC noted that the incremental cost effectiveness relies on benefits and costs that accrue 20 years or more in the future. The PBAC noted that the treatment of chronic hepatitis C is an evolving area which is likely to change substantially in the near future, which adds to the uncertainty in the long time horizon in the economic model.
- The transition probabilities. The PBAC noted that the model was highly sensitive to changes in the transition probabilities from mild to moderate HCV and from moderate HCV to compensated cirrhosis. The PBAC noted that the accuracy of available diagnostic methods and available treatments have changed over time and hence the data used in the model from studies published in 1985, 1989 and 1992 to estimate transition probabilities is likely to overestimate the likelihood of progression compared to present rates. Further, the PBAC noted that the route and source of infection may affect the rate of progression and that the studies used to estimate the transition probabilities had a much lower percentage of patients with community acquired HCV than in the Australian hepatitis C population today. The PBAC noted that this also was likely to result in an overestimation of the cost effectiveness of telaprevir.
- The utility values. Although noting there is variability in the utilities associated with hepatitis C in the published literature, the PBAC considered the utilities used in the submission from Wright 2006 tend to be lower than the values from other sources, and favour telaprevir.
- Re-infection is not captured in the model. The PBAC however noted the sensitivity analysis provided in the Pre-Sub-Committee Response (PSCR) of a 1.8 % re-

infection rate at two years, which did not result in a large change in the ICER. The PBAC accepted this was an appropriate sensitivity analysis because re-infection is most likely in the 3-5% of patients who actively continue intra-venous drug injecting and that the available data suggest a re-infection rate of 3-5/100 person years in this subgroup.

- The exclusion of telaprevir+PR induced anaemia, noting the sensitivity analyses presented in the PSCR.

Overall the PBAC considered the cost effectiveness was highly uncertain. The PBAC noted that the base case was in the range of $15,000 - $45,000/QALY for treatment naive patients and lower, yet within the same range for treatment experienced patients. However as outlined above, the PBAC considered many of the inputs to the economic model were likely to favour telaprevir+PR. The PBAC noted the sensitivity analyses presented in the PSCR where the three way sensitivity analysis with the utility associated with SVR reduced, the key transition probabilities reduced to half of those reported in the meta-analysis and the time horizon reduced to 30 years resulted in an ICER in the range of $45,000 - $75,000/QALY for treatment naive patients in the range of $15,000 - $45,000/QALY for treatment experienced patients.

The PBAC considered the utilisation estimates and hence the estimated financial cost to the PBS were highly uncertain. The PBAC considered the estimated uptake of telaprevir+PR to be uncertain, noting the current existing capacity constraints in HCV treatment infrastructure in Australia and that the treatment of chronic hepatitis C will change rapidly in the near future. The PBAC however considered that the submission's offsetting of 100 % of the estimated cost of PR use in treatment naïve genotype 1 chronic hepatitis C patients in the absence of telaprevir whilst estimating an uptake of 66.5 % of treated patients receiving telaprevir+PR, to be inappropriate.

The PBAC further noted the availability of interleukin (IL) 28B genotype (genotypes CC, CT and TT) testing on the private market. The PBAC noted that different IL28B genotypes may have a different response to treatment with telaprevir+PR, hence adding to the uncertainty in the cost effectiveness of telaprevir+PR.

The PBAC therefore considered that the cost-effectiveness ratio was highly uncertain and potentially unacceptably high and the utilisation estimates were also highly uncertain. The PBAC noted that the inputs to the economic model were the key sources of this uncertainty. However, the PBAC acknowledged that more applicable data to input into the model are not currently available. The PBAC also acknowledged the clinical need for additional treatment options for the treatment of chronic hepatitis C and noted the comment received from the Australian Liver Association, the Australasian Society for HIV Medicine and the Australasian Society for Infectious Diseases regarding the clinical place in therapy of telaprevir in the treatment of chronic hepatitis C.

The PBAC therefore deferred the submission so that discussion could take place with the sponsor regarding price, noting that a substantial further price reduction would be required in order to reduce the impact of uncertainty in the cost effectiveness ratio. The PBAC also considered that a Stakeholder meeting would be of benefit to more clearly ascertain the clinical place of telaprevir, the place of quantitative and qualitative HCV RNA and IL28B testing and to identify those patients who would most likely benefit from

this drug.

In making this recommendation the PBAC also noted the consumer comments on this item.

The PBAC noted the advice of the Highly Specialised Drugs Working Party (HSDWP) which did not support the listing of telaprevir as a HSD under Section 100 on the basis of not meeting criterion 2 (treatment of longer term medical conditions, not episodes of in-patient treatment or treatment of acute conditions) and criterion 4 (subject to marketing approval by the TGA and specific therapeutic indications covered by the terms of the marketing letter from the TGA). The PBAC did not agree with the advice of the HSDWP in relation to criterion 2, considering chronic hepatitis C to be a chronic (long term) medical condition and noting that telaprevir is indicated for use in combination with PR, with a treatment duration of combination therapy of 24 or 48 weeks.

Recommendation:
Defer

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

Janssen thank the PBAC for the invitation to attend the Hepatitis C stakeholder meeting and are also thankful to the PBAC and the Secretariat for making provisions to reconsider the protease inhibitors at the July 2012 PBAC meeting.