7.09 RIBAVIRIN tablets, 400mg and 600mg, Ibavyr®, Clinect Pty Ltd

1 Purpose of Application

1.1 The minor re-submission sought General Schedule (Section 85) listings for ribavirin, in combination with sofosbuvir, for the treatment of adults with chronic hepatitis C (CHC) genotype 2 or 3.

2 Requested listing

2.1 The re-submission requested the following new listings:

Requested PBS listing: initiation of treatment for previously untreated patients (Chronic genotype 2 or 3 hepatitis C infection)

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
RIBAVIRIN				Ibavyr® Clinect Pty Ltd
Tablets 400mg, 28	2	2	$[redacted]	
Tablets 600mg, 28	2	2	$[redacted]	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	–
Condition:	Chronic hepatitis C infection
PBS Indication:	Chronic hepatitis C infection
Treatment phase:	Initial treatment
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☒Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☒Streamlined
Treatment criteria:	Must be treated in an accredited treatment centre.
Clinical criteria:	Patient must have compensated liver disease. For patients with HCV genotype 2 infection: The treatment must be in combination with sofosbuvir only. For patients with HCV genotype 3 infection: The treatment must be in combination with sofosbuvir only.

Population criteria:	Patient must be 18 years or older. Patient must not be pregnant or breastfeeding. Female partners of male patients must not be pregnant. Patients and their partners must each be using an effective form of contraception if of child-bearing age.
Prescriber Instructions	Evidence of chronic hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive) must be documented in the patient's medical records.
Administrative Advice	Note: Increased repeats may be requested from the Department of Human Services for patients weighing equal to or greater than 75 kg Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C: a) a nurse educator/counsellor for patients; and b) 24-hour access by patients to medical advice; and c) an established liver clinic

Requested PBS listing: initiation of treatment for previously treated patients (Chronic genotype 2 or 3 hepatitis C infection)

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
RIBAVIRIN				Ibavyr® Clinect Pty Ltd
Tablets 400mg, 28	2	2	$[redacted]	
Tablets 600mg, 28	2	2	$[redacted]	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	–
Condition:	Chronic hepatitis C infection
PBS Indication:	Chronic hepatitis C infection
Treatment phase:	Initial treatment
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☒Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☒Streamlined
Treatment criteria:	Must be treated in an accredited treatment centre.

Clinical criteria:	Patient must have compensated liver disease. The patient must have received prior therapy with an interferon-based regimen. For patients with HCV genotype 2 infection: The treatment must be in combination with sofosbuvir only, For patients with HCV genotype 3 infection: The treatment must be in combination with sofosbuvir only,
Population criteria:	Patient must be 18 years or older. Patient must not be pregnant or breastfeeding. Female partners of male patients must not be pregnant. Patients and their partners must each be using an effective form of contraception if of child-bearing age.
Prescriber Instructions	Evidence of chronic hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive) must be documented in the patient's medical records.
Administrative Advice	Note: Increased repeats may be requested from the Department of Human Services for patients weighing equal to or greater than 75 kg Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C: a) a nurse educator/counsellor for patients; and b) 24-hour access by patients to medical advice; and c) an established liver clinic

Requested PBS listing: continuation of treatment (Chronic genotype 3 hepatitis C infection, patients electing 24 week regimen)

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
RIBAVIRIN				Ibavyr® Clinect Pty Ltd
Tablets 400mg, 28	2	2	$[redacted]	
Tablets 600mg, 28	2	2	$[redacted]	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	–
Condition:	Chronic hepatitis C infection
PBS Indication:	Chronic hepatitis C infection
Treatment phase:	Continuing treatment
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☒Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☒Streamlined

Treatment criteria:	Must be treated in an accredited treatment centre.
Clinical criteria:	Patient must have initiated ribavirin treatment under PBS Item number [TBC for initiation listing] for the first 12 weeks of the same course of treatment, The treatment must be in combination with sofosbuvir only.
Population criteria:	Patient must be 18 years or older. Patient must not be pregnant or breastfeeding. Female partners of male patients must not be pregnant. Patients and their partners must each be using an effective form of contraception if of child-bearing age.
Prescriber Instructions	Evidence of chronic hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive) must be documented in the patient's medical records.
Administrative Advice	Note: Increased repeats may be requested from the Department of Human Services for patients weighing equal to or greater than 75 kg Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C: a) a nurse educator/counsellor for patients; and b) 24-hour access by patients to medical advice; and c) an established liver clinic

2.2 The minor re-submission revised the requested listings for ribavirin to Section 85 (General schedule) listings as per PBAC advice that "it was appropriate that the new all oral treatment regimens be listed in the General Schedule, to facilitate the longer term objectives for access to treatment, increase treatment rates and outcomes with a view to treat all patients with CHC over time" (Paragraph 2.3, Item 5.21 Ribavirin, Ratified Minutes, March 2015 PBAC meeting). In addition, the re-submission proposed lower dispensed prices for maximum quantity (DPMQs) for ribavirin than those requested in the March 2015 submission (eg 600mg pack: $[redacted] vs $[redacted] (private hospital)). The proposed DPMQ included general schedule mark ups and fees and a [redacted]% reduction in the ex-manufacturer price.

The minor re-submission requested three listings for ribavirin (in combination with sofosbuvir): 1) for genotypes 2 and 3 treatment-naïve patients (initial treatment); 2) for genotypes 2 and 3 treatment-experienced patients (initial treatment); and 3) for genotype 3 HCV (continuing treatment). Apart from sofosbuvir, ribavirin has been used in combination with other direct-acting antivirals (DAAs) in various studies and recommended in American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) guidelines. At the March 2015 meeting, the PBAC noted that the ESC highlighted that there was evidence that ribavirin was used as adjunctive therapy to improve the sustained virologic response (SVR) or shorten treatment duration of DAA-based regimens (ribavirin PSD, March 2015).

For more detail on PBAC's view, see section 7 "PBAC outcome"

3 Background

3.1 Ribavirin was registered with the TGA in February 2015 for the treatment of CHC in adults, in combination with other oral agents.

3.2 A major submission for ribavirin for the treatment of genotypes 2 and 3 CHC (Section 100 (Highly Specialised Drugs Program) Authority Required (Streamlined) listing) was rejected by the PBAC at the March 2015 meeting, on the basis that the submission had not justified the incremental cost-effectiveness of ribavirin compared to the currently listed ribavirin-based items. The following table provides a summary of the key differences between the previous submission and the current re-submission, including PBAC comments on the March 2015 submission.

Table 1: Key differences between the March 2015 submission and the current minor re-submission

	March 2015 submission	Current re-submission
Requested listing	Section 100 listing for treatment of genotypes 2 and 3 CHC **PBAC comment:** It was appropriate that the new all oral treatment regimens be listed in the General Schedule.	General Schedule listing for treatment of genotypes 2 and 3 CHC
DPMQ	400mg x 28# x 2: $[redacted] (Public) $[redacted] (Private) 600mg x 28# x 2: $[redacted] (Public) $[redacted] (Private)	400mg x 28# x 2: $[redacted] 600mg x 28# x 2: $[redacted] The proposed DPMQ included general schedule mark ups and fees and a [redacted]% reduction in the ex-manufacturer price.
Economic analysis	The proposed prices for ribavirin were derived from external reference pricing. **PBAC comment:** • The approach presented in the submission, based on international reference pricing, was not informative for valuing ribavirin in the Australian context; • The PBAC noted that the submission presented an analysis of the 'shadow price' of ribavirin on the PBS. The PBAC considered that, though mathematically correct to use negative unit costs for deriving a weighted price, it was more appropriate to exclude negative costs in this analysis; • The PBAC were of a mind to approve listing if stand-alone ribavirin was cost-minimised to the ribavirin in the co-pack with peginterferon most likely to be replaced, based on current usage, and if the cost of the total treatment course remained in the acceptable willingness-to-pay threshold for a CHC patient weighting less than 75kg; and • The PBAC noted that the Commentary stated that an alternative approach to determine the ribavirin price could have been to establish the cost-effective price for SOF+R as a combination therapy and then suggest a negotiation between the sponsors of the two products with regard to the disaggregated reimbursed prices for sofosbuvir and ribavirin that they would be willing to have	The requested prices for ribavirin were determined on a cost-minimisation basis to the component of cost attributable to ribavirin within Pegasys RBV® [redacted] (Table 2). Not from the submission, a weighted shadow price for ribavirin was calculated according to PBAC advice, ie [redacted] (Table 3).

	March 2015 submission	Current re-submission
	listed on the PBS. • During consideration of sofosubvir, daclatasvir and ledipasvir/sofosbuvir at the March 2015 meeting, the PBAC advised the Minister that there was no basis on which to recommend that any one treatment be more expensive than another.	
Financial analysis	Number of patients likely to receive ribavirin: less than 10,000 in Year 1, increasing to less than 10,000 in Year 5 Net costs to the PBS: less than $10 million in Year 1, increasing to between $10-$20 million in Year 5 **PBAC comment:** • The PBAC noted the estimates by DUSC, during the consideration of items 5.03, 5.06, 5.13 and 7.04. The number of patients of all genotypes estimated to be treated over the first five years of listing of new treatments would be less than 10,000 in Year 1, increasing to 10,000-50,000 in Year 5 (higher than the submission's estimate (less than 10,000)). • The PBAC considered that the advice received from the Australian Liver Association, namely Bruggmann *et al*. (2014), was the most appropriate source of HCV genotype distribution in Australia. • The submission's estimate of the proportion of patients with genotype 3 CHC seeking an interferon-free treatment of SOF+R (66.8%) was considered an underestimate. The PBAC agreed with ESC and DUSC and considered more appropriate to assume 100% of genotype 3 HCV patients will seek SOF+R.	Number of patients likely to receive ribavirin: less than 10,000 in Year 1, increasing to less than 10,000 in Year 5. Net costs to the PBS: less than $10 million in Year 1, increasing to between $10 - $20 million in Year 5 PBAC's suggestions for determination of the financial implications associated with the proposed listing of ribavirin have been accepted in full.

CHC = chronic hepatitis C; DPMQ = dispensed price for maximum quantity; HCV = hepatitis C virus; SOF+R = sofosbuvir + ribavirin

Source: Table compiled for the purpose of the Overview, based on ribavirin submissions and the March 2015 Ratified PBAC Minutes for ribavirin.

4 Clinical place for the proposed therapy

4.1 In Australia, ribavirin has not been listed as a stand-alone medicine on the PBS and is only available within a combination package with peginterferon alfa-2a (Pegasys RBV®) or peginterferon alfa-2b (Pegatron®). The PBAC has previously noted the clinical need for a stand-alone ribavirin for the treatment of genotypes 2 and 3 patients if sofosbuvir is listed on the PBS (ribavirin PSD, March 2015). Apart from sofosbuvir, ribavirin has been used in combination with other direct-acting antivirals (DAAs) in various studies and recommended in guidelines[4]. (Additional information in the "Committee-In-Confidence information" section). At the March 2015 meeting, the PBAC noted that the ESC highlighted that there was evidence that ribavirin was used as adjunctive therapy to improve the sustained virologic response (SVR) or shorten treatment duration of DAA-based regimens (ribavirin PSD, March 2015).

5 Comparator

5.1 The minor re-submission agreed with the PBAC that 'no treatment' was the most appropriate comparator in view of the broader context of infected individuals whose treatment preference is interferon-free therapies (ribavirin PSDs, March 2015).

6 Consideration of the evidence

Sponsor hearing

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

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (78), health care professionals (14) and organisations (17) via the Consumer Comments facility on the PBS website. The large number of comments and discussion reiterate the comments received during previous considerations of the IFN-free treatments, namely the benefit of the availability of a highly effective treatment that should be made available for all infected individuals, the improved quality of life as well as the side effects avoided associated with the current treatments.

6.3 The PBAC recalled the discussion during meeting of the representatives of the PBAC with Hepatitis Australia, Hepatitis NSW, the Australian Injecting and the Illicit Drug User's League prior to the March 2015 PBAC meeting.

6.4 The PBAC noted and welcomed this input.

Clinical trials

6.5 As in the previous submission, no clinical data were presented in the re-submission.

Economic analysis

6.6 The March 2015 ribavirin submission referred to the sofosbuvir submission for cost-utility analyses of sofosbuvir + ribavirin (SOF+R) in the intended PBS population. The proposed price for ribavirin in the previous submission was not based on any economic analysis; it was derived from international reference pricing. The PBAC considered that this approach was not informative for valuing ribavirin in the Australian context (ribavirin PSD, March 2015).

~~6.7~~ In the minor re-submission, the requested price for ribavirin (ex-manufacturer price of $[redacted] per 200mg ribavirin) was determined via an assessment of the cost attributable to ribavirin within Pegasys RBV® [redacted]

- At the June 2003 PBAC meeting, Pegasys RBV® was recommended for treatment of CHC on a cost-minimisation basis against Pegatron®, with implicit cost-effectiveness, as Pegatron® had been listed on the PBS on a cost-effectiveness basis for patients with HCV genotypes 1, 4, 5 or 6 and on a cost-minimisation basis for patients with genotypes 2 or 3 against non-pegylated interferon alfa-2b plus ribavirin (Rebetron®). As stated in the Therapeutic Relativity Sheets (December 2014), "Peginterferon alfa-2a and ribavirin (Pegasys RBV®) for use in hepatitis C patients who have had no prior interferon therapy, was recommended on the basis of acceptable cost-effectiveness compared to plain (non-pegylated) interferon alfa therapy"; and
- [redacted].

Table 2: Pricing of ribavirin within Pegasys-RBV® combination on listing in 2004/2005[a]

Pegasys®								
Pegasys dose	135µg				180µg			
Price	$[redacted]				$[redacted]			
Pegasys RBV®								
Pegasys dose	135µg				180µg			
No. of ribavirin 200mg tablets	84	112	140	168	84	112	140	168
Price	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
'Shadow price' for ribavirin per 200mg tablet	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**

[a] Although Pegasys RBV appeared on the PBS in February 2004, Pegasys alone did not appear until April 2005; hence the analysis has been based on April 2005 ex-manufacturer prices. The price of Pegasys RBV did not change between February 2004 and April 2005.
Source: Table 7, p16 of the minor re-submission.

6.8 When considering the original ribavirin submission, the PBAC "were of a mind to approve listing if stand-alone ribavirin was cost-minimised to the ribavirin in the co-pack with peginterferon most likely to be replaced, based on current usage…" (ribavirin PSD, March 2015). The PBAC also noted the negative shadow price for ribavirin and "considered that, though mathematically correct to use negative unit costs for deriving a weighted price, it was more appropriate to exclude negative costs in this analysis" (ribavirin PSD, March 2015). The current weighted ex-manufacturer shadow price for ribavirin, excluding the negative values, was estimated to be $[redacted] per 200mg tablet (Table 3). The re-submission strongly re-affirmed that the PBAC's suggested approach to calculation of the shadow price for ribavirin was "not only mathematically invalid, but inconsistent with all other approaches taken to cost analysis for the purposes of PBS listing".

Table 3: Weighted average 'shadow price' per 200 mg tablet of ribavirin

PBS item (Public)	PBS item (Private)	Pack	'Shadow price' per 200mg tablet[a]	PBS Services (2013-2014)	Ribavirin units (200mg tablets)	*Weighted average per 200mg tablet*
Pegasys RBV®						
9524g	6392k	135/168	$[redacted]	163	27,384	
9525h	6394m	180/112	$[redacted]	4039	452,368	
9526j	6395n	180/140	$[redacted]	3438	481,320	
9527k	6396p	180/168	$[redacted]	5041	846,888	
Pegatron®						
9529m	6400w	50/112	$[redacted]	30	3,360	
TOTAL					1,811,320	***$[redacted]***

[a] Calculated using the ex-manufacturer prices listed on the PBS as in May 2015

[b] The peginterferon component in the Pegatron® co-pack (Peg-Intron®) was delisted in 2012. As the price for Peg-Intron® had not changed since its listing, the price for Peg-Intron® in 2011 was used for determination of the ribavirin shadow price.

Source: Weighted shadow price calculated according to previous PBAC advice (ribavirin PSD, March 2015).

6.9 Stand-alone ribavirin, at its requested price, was not considered to be cost-minimised to the product most likely to be substituted, ie the ribavirin component in the co-packaged Pegasys RBV® and Pegatron®, at their current prices ($[redacted] vs $[redacted] per 200mg ribavirin).

6.10 The pricing of ribavirin was also considered in relation to the price for the co-administered sofosbuvir. At the March 2015 meeting, the PBAC noted that, to be listed on the PBAC, not only should ribavirin be cost-minimising to the ribavirin component in the co-packaged PR, but the cost of the total treatment course (12-week and 24-week SOF+R) should also remain "in the acceptable willingness-to-pay threshold for a CHC patient weighting less than 75kg" (ribavirin PSD, March 2015).

6.11 The minor re-submission reiterated that the estimation of the portion of efficacy attributable to ribavirin was not feasible within the available medical and pharmacological knowledge or from the clinical data on ribavirin in various combination regimens. Therefore, it was claimed to be impossible to model the cost-effectiveness of the ribavirin component of the SOF+R combination, which would have required an evaluation of both the incremental costs of adding ribavirin to sofosbuvir and the incremental health gain (clinical evidence not available).

6.12 The PBAC recalled that daclatasivr in combination with sofosbuvir and sofosbuvir (when in combination with ribavirin) were recommended for the treatment of CHC at the March 2015 meeting. During the consideration of daclatasivr in combination with sofosbuvir for the treatment of Genotype 3 patients, the listing was recommended on the basis of acceptable cost effectiveness over no treatment, however the PBAC recommended that the price of a course of treatment should be the same as the price of a course of treatment with sofosbuvir in combination with ribavirin (24 weeks), as presented in the sofosbuvir resubmission.

6.13 The PBAC noted that the proposed DPMQ in the submission included general schedule mark ups and fees in line with the previous view of the PBAC for listing of all oral CHC treatments.

6.14 The PBAC recalled from the March 2015 meeting, in consideration of CHC treatments, that:

- the cost of the entire treatment course would be required to give an ICER no greater than $15,000/QALY based on the model presented in the sofsobuvir resubmission,
- the most appropriate scenario to determine the cost of a treatment would be based on the largest groups of the total prevalent population, namely treatment naïve non-cirrhotic Genotype 3 patients (weighing less than 75kg) treated with SOF+ RBV 24 weeks as a proxy for all Genotype 3, 2, 4, 5 and 6 patients.

- the cost of the entire treatment course should include the wholesale and pharmacy mark ups and dispensing fees associated with a General Schedule listing.
- the cost to achieve a SVR12 should be independent of the treatment duration and treatment dose considered to be appropriate to achieve a SVR in patients.

6.15 Overall, the PBAC considered with the clinical evidence available in the public domain that there was no basis on which to recommend that any one treatment (including those that are in combination with ribavirin) was more effective and thus be more expensive than another.

Drug cost/patient/course

6.16 The costs for ribavirin using the requested DPMQs were estimated in the submission to be:

- $[redacted] for the 12-week regimen for patients weighing <75kg;
- $[redacted] for the 12-week regimen for patients weighing ≥75kg;
- $[redacted] for the 24-week regimen for patients weighing <75kg; and
- $[redacted] for the 24-week regimen for patients weighing ≥75kg.

Estimated PBS usage & financial implications

6.17 The re-submission provided an update of the financial implications associated with the proposed listing of ribavirin.

6.18 The re-submission's approach to estimating the extent of use of ribavirin was largely consistent with that in the March 2015 submission, with some assumptions revised:

- The re-submission used the DUSC's estimate of the number of CHC patients (all genotypes) likely to receive interferon-free therapies: 6,600 in Year 1 of listing, increasing to and remaining 15,000 per year from Year 3 (Paragraph 6.14, Item 5.21 Ribavirin, Public Summary Document, March 2015 PBAC meeting);
- The genotype distribution in the treated Australian CHC population was sourced from Bruggmann *et al* 2014[3] as per PBAC advice (Paragraph 6.12, Item 5.21 Ribavirin, Public Summary Document, March 2015 PBAC meeting);

- The proportion of patients with genotype 3 HCV seeking an interferon-free treatment of SOF+R was estimated to be 66.7% (the remaining 33.3% receiving interferon-containing regimen of SOF+PR) in the previous March 2015 submission. The PBAC considered this an underestimate in the context of known patient preferences for an interferon-free regimen (Paragraph 6.11, Item 5.21 Ribavirin, Public Summary Document, March 2015 PBAC meeting). The minor re-submission assumed a 100% of genotype 3 HCV patients will seek the interferon-free regimen of SOF+R; and
- The re-submission assumed a higher percentage of patients weighing ≥75kg than that estimated in the previous submission (50% *vs* 33%). This is consistent with the Commentary on the previous submission (5.21.COM.26).

6.19 The redacted table below shows that the number of patients likely to receive ribavirin was estimated to be 10,000 – 50,000 over the first 5 years of listing. The minor re-submission estimated a net cost to the PBS/RPBS of $10 – 20 million in Year 5 of listing, with a total net cost to the PBS of $60-$100 million over the first 5 years of listing. Of note: these estimates did not include the cost of co-administered sofosbuvir and the cost offset arising from the substitution of current active treatments (only in a small proportion of the target population).

Table 4: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Over 5 years
Extent of use						
Number treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of prescripts	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Financial implications						
Net costs to the PBS/RPBS (less co-payments)[a]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net costs to government health budgets[b]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

[a] The re-submission did not estimate changes in costs of other drugs, *eg* sofosbuvir and current active treatments
[b] The re-submission did not estimate the potential incremental costs or savings to other government health budgets associated with the proposed listing of ribavirin.
Source: Table 10, p22 and Table 11, p23 of the minor re-submission

6.20 The minor re-submission also presented a financial analysis in a scenario where sofosbuvir was listed on the PBS, in the absence of a listing of single agent ribavirin, and patients receiving SOF+R were prescribed the PBS-listed co-packaged PR to access ribavirin. For simplicity, this analysis was based on DPMQ prices (including patient co-payments). Assuming that all patients treated with SOF+R would be prescribed co-packaged PR and discard the peginterferon component if stand-alone ribavirin is not available, the proposed listing of ribavirin would result in a cost saving of up to around $30 - $60 million in Year 5 of listing.

For more detail on PBAC's view, see section 7 "PBAC outcome"

7 PBAC Outcome

7.1 The PBAC deferred its decision for the Authority Required listing of ribavirin for the treatment of chronic hepatitis C (CHC).

7.2 The PBAC reiterated the clinical need for stand-alone ribavirin (RBV) for the treatment of genotype 2 and 3 patients, noting the large number of comments and presentations from patients, health care professionals and organisations highlighted the benefits of the availability of new treatments, particularly IFN-free regimens.

7.3 The PBAC recalled daclatasivr in combination with sofosbuvir and sofosbuvir (when in combination with ribavirin, SOF + R) were recommended for the treatment of CHC at the March 2015 meeting.

7.4 The PBAC reiterated that it was appropriate that the new all oral treatment regimens be listed in the General Schedule, to facilitate the longer term objectives for access to treatment, increase treatment rates and outcomes with a view to treat all patients with CHC over time. The PBAC noted that the resubmission requested a General Schedule listing.

7.5 The PBAC noted the submission's proposal that 'no treatment' was the most appropriate comparator in accordance with the previous PBAC consideration that in the broader context of HCV treatments, the appropriate comparator for the newer IFN-free regimens is no treatment (ribavirin PSD, March 2015). Following the recommendation to list sofosbuvir-containing regimens, the PBAC considered that these sofosbuvir-containing regimens were the most appropriate comparators for the consideration of all other oral HCV treatments, given that LDV/SOF and SOF are likely to become the standard of care for almost all patients treated for CHC.

7.6 The PBAC noted that no new clinical data were presented in the re-submission and recalled that the submission lodged for the March 2015 consideration did not provide any clinical evidence in support of the combination treatment of SOF+R for treatment of genotypes 2 and 3 HCV infection, but referred to the sofosbuvir submission considered at the July 2014 PBAC meeting for relevant data on the effectiveness and safety of SOF+R in the proposed PBS population. The PBAC has accepted the clinical benefit of this treatment regimen for treating genotypes 2 and 3 HCV infection.

7.7 The PBAC considered with the clinical evidence available that there was no basis on which to recommend that any one treatment (including those that are in combination with ribavirin) be more expensive than another.

7.8 In the context of the number of IFN-free treatments for CHC that have been recently assessed by the TGA and considered by the PBAC for the listing on the PBS, the PBAC considered that the most appropriate way in which to make subsidised ribavirin available in Australia is uncertain, noting that:

- this submission requested the General Schedule listing for ribavirin, in combination with sofosbuvir, for the treatment of adults with chronic hepatitis C (CHC) genotype 2 or 3.
- the dosage and administration section of the product information for daclatatasvir (DATE OF INCLUSION IN THE ARTG 25 June 2015) states 'Consider adding ribavirin to the DAKLINZA/sofosbuvir 12-week regimen or prolonging treatment duration to 24 weeks for patients with cirrhosis' in Genotype 1 patients.

- international guidelines, such as from American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) recommend ribavirin to be used in combination with other direct-acting antivirals (DAAs), including sofosbuvir used in combination with simeprevir

7.9 The PBAC was concerned that how ribavirin would be used in association with other all oral interferon-free regimens in Australia, compared to other international guidelines, has not been established and that the proposed listing may inappropriately restrict availability of ribavirin to patients infected with other CHC genotypes.

7.10 The PBAC noted the submission's approach to estimate the extent of use of ribavirin based on the PBAC's March recommendations regarding the number of CHC patients (all genotypes) likely to receive interferon-free therapies. The PBAC noted the submission's estimates of the likely number of patients using ribavirin to be10,000-50,000, resulting in a net cost of up to $60 - $100 million, based on the proposed price over 5 years. The PBAC noted that these estimates would be part of the larger financial implication of the listing of IFN-free treatments for CHC.

7.11 The submission is not eligible for an Independent Review, because the decision by the PBAC has been deferred.

Outcome:
Deferred.

8 Context for decision

The PBAC helps decide whether an, 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.

9 Sponsor's Comment

The sponsor was disappointed that the significantly revised pricing proposed in its resubmission, which was demonstrably based on a previously accepted cost minimisation outcome, was again not accepted by the PBAC.

The PBAC states 'uncertainty' about how to make ribavirin available for future CHC treatments. However the proposed listing of ribavirin is reflective of the current approved treatment regimens presented for consideration at this cycle. If the 'stepwise' approach to listings, as discussed at prior CHC Stakeholder meetings is adopted to meet the evolution of CHC therapy, the stand alone ribavirin listing could be extended accordingly by the PBAC and sponsor. The TGA approved indication of IBAVYR® is for 'the treatment of CHC in adults, in combination with other oral agents' and should present no obstacle in such a process.

The sponsor remains committed to working with the PBAC to secure reimbursement of IBAVYR® to assist Australians suffering with Chronic Hepatitis C.