

**5.11 PARITAPREVIR with RITONAVIR and OMBITASVIR,
Tablet containing 75 mg paritaprevir with 50 mg ritonavir and
12.5 mg ombitasvir,
Technivie[®],
AbbVie Pty Ltd.**

1 Purpose of Application

1.1 The submission requested a General Schedule and Section 100 Authority Required listing for the fixed dose combination (FDC) of paritaprevir 75 mg, ritonavir 50 mg and ombitasvir 12.5 mg (herein referred to as Technivie[®]) in combination with ribavirin (RBV) for treatment of patients infected with genotype 4 (GT4) chronic hepatitis C (CHC), irrespective of previous treatment history. RBV is to be dispensed separately via the Pharmaceutical Benefits Scheme (PBS) and will not be co-packaged with Technivie[®].

2 Requested listing

2.1 The requested listings are provided below. The Secretariat proposed the addition of notes consistent with other drugs supplied under the *General Statement for Drugs for the Treatment of Hepatitis C* (no increase in the maximum quantity, number of units or repeats may be authorised). The Secretariat also proposed that the prescriber type should include medical practitioners experienced in the treatment of hepatitis C, in line with changes to the *General Statement* that were implemented on 1 November 2016. In addition, the Secretariat proposed that the pregnancy caution below need not apply to Technivie[®] (Category B3), since this is already included on all PBS RBV listings (Category X).

Name, Restriction, Manner of administration and form	Max. Qty (units)	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
PARITAPREVIR/RITONAVIR AND OMBITASVIR Tablets 75/50/12.5mg	56	2	\$ [REDACTED]*	Technivie [®] AbbVie Pty Ltd

Section 85 and Section 100 (Authority Required)

Treatment phase:	
Duration	12 weeks of treatment for all patients
Condition	Genotype 4, Chronic Hepatitis C infection
Clinical criteria	Patient must meet the criteria set out in the General Statement for Drugs for the Treatment of Hepatitis C; AND Patient must be taking this drug as part of a regimen set out in the matrix in the General Statement for Drugs for the Treatment of Hepatitis C, based on the hepatitis C virus genotype, patient treatment history and cirrhotic status; AND The treatment must be limited to a maximum duration of 12 weeks.
Population criteria	Patient must be aged 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.

Treatment criteria (as per General Statement for Drugs for the Treatment of Hepatitis C)	<p>Must be treated by a gastroenterologist, hepatologist or infectious diseases physician experienced in the treatment of chronic hepatitis C infection; or in consultation with a gastroenterologist, hepatologist or infectious diseases physician experienced in the treatment of chronic hepatitis C infection.</p> <p>The following information must be provided at the time of application:</p> <p>a) the hepatitis C virus genotype; and b) the patient's cirrhotic status (non-cirrhotic or cirrhotic)</p> <p>The following information must be documented in the patient's medical records:</p> <p>a) evidence of chronic hepatitis C infection (repeatedly antibody to hepatitis C virus (anti-HCV) positive and hepatitis C virus ribonucleic acid (HCV RNA) positive); and b) evidence of the hepatitis C virus genotype</p>
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Treatment Matrix:		
Hepatitis C-Non-cirrhotic patients		
Genotype 4	Treatment Naïve	Treatment Experienced
	PARITAPREVIR + RITONAVIR + OMBITASVIR and RBV [12 weeks]	PARITAPREVIR + RITONAVIR + OMBITASVIR and RBV [12 weeks]
Hepatitis C-Cirrhotic patients		
Genotype 4	Treatment Naïve	Treatment Experienced
	PARITAPREVIR + RITONAVIR + OMBITASVIR and RBV [12 weeks]	PARITAPREVIR + RITONAVIR + OMBITASVIR and RBV [12 weeks]

* Price is the published DPMQ. The sponsor has proposed a confidential effective DPMQ of \$ [REDACTED] per pack.

- 2.2 Listing of Technivie®+RBV was initially sought on a cost-effectiveness and cost-utility basis compared with 'no treatment'.
- 2.3 The sponsor subsequently indicated a willingness to list Technivie® + RBV on a cost-minimisation basis to grazoprevir-elbasvir ± ribavirin (GZR-EBR ± RBV), which was considered at the July 2016 PBAC meeting and received a positive recommendation for listing. The cost-minimisation checklist for this comparison was completed during the evaluation.
- 2.4 The ESC noted the updated draft Product Information (PI) (13 September 2016) provided with the Pre-Sub-Committee Response (PSCR), which stated that use of Technivie® is not recommended in patients with moderate hepatic impairment (Child-Pugh B) and is contraindicated in patients with severe hepatic impairment (Child-Pugh C). The ESC noted that the TGA-approved PIs for PBS-listed Viekira Pak® and Viekira Pak-RBV® have also recently been updated to include these additional statements (see also paragraphs 6.23 – 6.27 and 6.40 – 6.41).

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

3 Background

- 3.1 **TGA status at time of PBAC consideration:** The submission was made under the TGA/PBAC Parallel Process. Technivie® was considered at the 312th ACPM meeting on 7 October 2016, and the draft ACPM resolution was available at the time of the PBAC meeting. At the time of the ESC meeting, the TGA Delegate's Overview, and updated draft Product Information (dated 13 September 2016) were available. At the time of evaluation, the Clinical Evaluation Reports Round 1 and 2 were available.

- 3.2 This was the first submission of Technivie® to the PBAC. A similar FDC is currently listed on the PBS (paritaprevir/ritonavir/ombitasvir and dasabuvir ± ribavirin (Viekira PAK® and Viekira Pak-RBV®)) for genotype 1 (GT1) HCV. It contains the same active ingredients with the exception of dasabuvir, which has no activity against GT4 HCV. Viekira Pak® and Viekira Pak-RBV® were recommended at the July 2015 PBAC meeting.
- 3.3 GZR-EBR ± RBV received a positive recommendation for listing at the July 2016 PBAC meeting for the treatment of GT4, chronic hepatitis C infection. At the time of the November 2016 PBAC meeting, GZR-EBR ± RBV was not PBS listed for this use.

4 Clinical place for the proposed therapy

- 4.1 Hepatitis C is a blood-borne inflammatory liver disease caused by the hepatitis C virus (HCV), with approximately 75-80% of people exposed to HCV developing chronic hepatitis C infection which may lead to cirrhosis, liver failure, hepatocellular carcinoma and death. In Australia, approximately 230,000 people were estimated to be living with chronic HCV infection in 2014 (Kirby 2015), of which 2% would have genotype 4 (GT4) infection (Bruggmann 2014).
- 4.2 Technivie® is a peginterferon-free direct acting antiviral (DAA). Prior to the PBAC July 2016 recommendation for GZR-EBR ± RBV, sofosbuvir plus peginterferon + ribavirin 12 weeks (SOF + PR) was the only treatment regimen for GT4 CHC recommended for listing on the PBS. The PBAC noted that GZR-EBR is contraindicated in some patients who may be able to use Technivie® + RBV.

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

5 Comparator

- 5.1 The nominated main comparator was initially 'no treatment'. Supportive comparators were GZR-EBR ± RBV and SOF + PR. Clinical comparisons were presented against both supportive comparators, plus a modelled economic evaluation versus 'no treatment', assuming zero sustained virologic response (SVR) for those not receiving treatment.
- 5.2 The PBAC considered that GZR-EBR ± RBV was the most appropriate comparator on the basis that it is the therapy most likely to be replaced in clinical practice.

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 There was no hearing for this item.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (3) and organisations (10) via the Consumer Comments facility on the PBS website. The comments described how this [class of] drug will improve cure rates, reduce treatment duration and offer simpler administration with fewer side effects. The comments also noted that increased treatment of hepatitis C infection will reduce the risk of transmission within the community.
- 6.3 The PBAC noted the advice received from the following organisations with regards to the three submissions for chronic hepatitis C treatment made to the PBAC at this meeting [this submission and items 5.14 sofosbuvir + velpatasvir and 6.03 ledipasvir + sofosbuvir]:
- Hepatitis Australia
 - Haemophilia Foundation Australia
 - Hepatitis NSW
 - ACON
 - The Haymarket Foundation
 - Hepatitis ACT
 - Network of Alcohol and Other Drugs Agencies
 - Sex Workers Outreach Project
 - St Vincent de Paul Society NSW
 - We Help Ourselves

The PBAC noted the view shared amongst most organisations that these new treatments will help ensure as many GPs as possible are able to prescribe the new direct acting antivirals, that all people living with hepatitis C have access to interferon-free treatment, and that there are multiple treatment options for each hepatitis C genotype. The PBAC also noted the advice that there are certain populations living with both HCV and other health conditions, and that successful treatment of HCV would greatly reduce the complexity of the healthcare needs of these groups.

Clinical trials

- 6.4 No head to head trials comparing Technivie® versus any of the nominated comparators were identified. The submission was based on:
- three Technivie® trials (PEARL I, AGATE I and AGATE II);
 - four GZR-EBR studies (C-EDGE TN, C-EDGE COINFECTION, C-SCAPE and C-EDGE TE); the results for an additional study (C-EDGE CO-STAR) identified during the evaluation were incorporated into the Commentary; and
 - one SOF + RBV study (NEUTRINO); Wehmeyer (2015), identified during the evaluation, was also included in the Commentary.
- 6.5 Details of the studies included in the submission are presented in Table 1. All studies were treated as non-comparative single arm studies with respect to the estimation of sustained virological response.

Table 1: Studies and associated reports presented in the submission (and identified during the evaluation)

Study ID	Protocol title/ Publication title	Publication citation
Technivie® plus ribavirin		
PEARL I NCT01685203	Clinical Study Report: A Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Coadministration of ABT-450 with Ritonavir (ABT-450/r) and ABT-267 in Adults with Chronic Hepatitis C Virus Infection (PEARL-I)	30 September 2014
	Hézode C, Asselah T, Reddy KR, <i>et al.</i> Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin in treatment-naïve and treatment-experienced patients with genotype 4 chronic hepatitis C virus infection (PEARL-I): A randomised, open-label trial.	<i>Lancet</i> 2015; 385(9986): 2502-9. doi: http://dx.doi.org/10.1016/S0140-6736(15)60159-3 .
AGATE I NCT02265237	Clinical Study Report: A Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Ombitasvir/ABT-450/Ritonavir Co-administered with Ribavirin (RBV) in Adults with Genotype 4 Chronic Hepatitis C Virus (HCV) Infection and Cirrhosis (AGATE-I)	2 March 2016
	Asselah T, Hézode C, Qaqish RB, <i>et al.</i> Ombitasvir, paritaprevir, and ritonavir plus ribavirin in adults with hepatitis C virus genotype 4 infection and cirrhosis (AGATE-I): a multicentre, phase 3, randomised open-label trial. ^a	<i>Lancet Gastroenterol Hepatol</i> 2016; 1: 25-35.
AGATE II NCT02247401	Clinical Study Report not yet available	
	Waked I, Shiha G, Qaqish RB, <i>et al.</i> Ombitasvir, paritaprevir, and ritonavir plus ribavirin for chronic hepatitis C virus genotype 4 infection in Egyptian patients with or without compensated cirrhosis (AGATE-II): a multicentre, phase 3, partly randomised open-label trial. ^a	<i>Lancet Gastroenterol Hepatol</i> 2016; 1: 36–44.
Grazoprevir-elbasvir ± ribavirin		
C-EDGE TN NCT02252016	Zeuzem S, Ghalib R, Reddy KR, <i>et al.</i> Grazoprevir-elbasvir combination therapy for treatment-naïve cirrhotic and noncirrhotic patients with chronic hepatitis C virus genotype 1, 4, or 6 infection: A randomized trial.	<i>Ann Intern Med</i> 2015; 163(1): 1-13. doi: http://dx.doi.org/10.7326/M15-0785 .
	Kwo P, Gane E, Peng C-, <i>et al.</i> Efficacy and safety of grazoprevir/elbasvir plus /- rbv for 12 weeks in patients with HCV G1 or G4 infection who previously failed peginterferon/rbv: c-edge treatment-experienced trial.	<i>J Hepatol</i> 2015; 62: S674-S675.
C-EDGE CO-INFECTION NCT02105662	Rockstroh J, Nelson M, Katlama C, <i>et al.</i> Efficacy and safety of grazoprevir (MK-5172) and elbasvir (MK-8742) in patients with hepatitis C virus and HIV co-infection (C-EDGE CO-INFECTION): A non-randomised, open-label trial.	<i>Lancet HIV</i> 2015; 2(8): e319-e327. doi: http://dx.doi.org/10.1016/S2352-3018(15)00114-9 .
C-SCAPE NCT01932762	Brown A, Hezode C, Zuckerman E, <i>et al.</i> C-SCAPE: Efficacy And Safety Of 12 Weeks Of Grazoprevir Plus /- Elbasvir Plus /- Ribavirin In Patients With HCV GT2, 4, 5 Or 6 Infection.	<i>J Hepatol</i> 2015; 62: S619.
C-EDGE CO-STAR ^a NCT02105688	Dore GJ, Altice F, Litwin AH, <i>et al.</i> Elbasvir–Grazoprevir to Treat Hepatitis C Virus Infection in Persons Receiving Opioid Agonist Therapy: A Randomized Trial. ^a	<i>Ann Intern Med Published online 9 August 2016; doi:10.7326/M16-0816</i> .
Sofosbuvir plus peginterferon plus ribavirin (supplementary study)		
NEUTRINO NCT01641640	Lawitz E, Mangia A, Wyles D, <i>et al.</i> Sofosbuvir for Previously Untreated Chronic Hepatitis C Infection.	<i>N Engl J Med</i> 2013; 368: 1878-87. DOI: 10.1056/NEJMoa1214853
	Stepanova M, Nader F, Cure S, <i>et al.</i> Patients' preferences and health utility assessment with SF-6D and EQ-5D in patients with chronic hepatitis C treated with sofosbuvir regimens.	<i>Aliment Pharmacol Ther</i> 2014; 40(6): 676-685.
	Younossi ZM, Stepanova M, Henry L, <i>et al.</i> Effects of sofosbuvir-based treatment, with and without interferon, on outcome and productivity of patients with chronic hepatitis C.	<i>Clin Gastroenterol Hepatol</i> 2014; 12(8): 1349-59.e13.
Wehmeyer 2015 ^a	Wehmeyer M., Jordan S., Lütha S., <i>et al.</i> Efficacy and safety of sofosbuvir-based triple therapy in hepatitis C genotype 4 infection ^a	<i>Digestive and Liver Disease</i> 2015; 47: 811–814.

^a Trial and/or report identified during the evaluation.

Note: Abstracts/presentations of conference proceedings were not included if a relevant peer-reviewed journal article was available. Technivie® represents treatment with paritaprevir/ritonavir/ombitasvir.

Source: Table B-3, pp69-71 of the submission

6.6 The key features of the included studies are summarised in Table 2.

Table 2: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias ^d	Tx arm	n	Patient population			Tx	Tx duration (weeks)	Key outcome
						HCV Gt	Cirrhosis ^a	Tx history			
Technivie® + ribavirin											
PEARL I	316	R, OL, MC, Phase II	NA	1	44	4	No	Naïve	Technivie®	12	SVR12
				4	42	4	No	Naïve	Technivie® +RBV	12	
				6	49	4	No	Experienced	Technivie® +RBV	12	
AGATE I (part 1)	148	R, OL, MC, Phase III	NA	A	59	4	Yes	Naïve or experienced	Technivie® +RBV	12	SVR12
				B	61	4	Yes	Naïve or experienced	Technivie® +RBV	16	
AGATE II	160	R, OL, MC (Egypt), Phase III	NA	A	100	4	No	Naïve or experienced	Technivie® +RBV	12	SVR12
				B	31	4	Yes	Naïve or experienced	Technivie® +RBV	12	
				C	29	4	Yes	Naïve or experienced	Technivie® +RBV	24	
Grazoprevir-elbasvir ± ribavirin											
C-EDGE TN	421	R, DB, MC, Phase III (deferred Tx– OL CO for PBO)	NA	ITG	316	1, 4, 6	Mixed	Naïve	GRZ/EBR	12	SVR12
Gt 4 subgp	26			ITG	18	4	Mixed	Naïve	GRZ/EBR	12	
C-EDGE TE	420	R, OL, MC, Phase III	NA	D	106	1, 4, 6	Mixed	Experienced	GRZ/EBR+ RBV	16	SVR12
Gt 4 subgp	37			D	8	4	Mixed	Experienced	GRZ/EBR+ RBV	16	
C-EDGE CO- INFECTION	218	OL, MC, single arm, Phase III	NA	-	218	HCV/HIV-1 co-infection			GRZ/EBR	12	SVR12
Gt 4 subgp	28			-	28	4	Mixed	Naïve			
C-SCAPE	98	R, MC Phase II	NA	B3	19	4, 5, 6	No	Naïve	GRZ/EBR	12	SVR12
Gt 4 subgp	20			B3	10	4	No	Naïve	GRZ/EBR	12	
C-EDGE CO-STAR ^d	301	R, DB, MC (deferred Tx– OL CO for PBO for DTG)	NA	-	-	Persons who inject drugs			-	-	SVR12
Gt 4 subgp ^d	18			ITG	201	1, 4, 6	Mixed	Naïve	GRZ/EBR	12	
				DTG	100 ^b	1, 4, 6	Mixed	Naïve	GRZ/EBR	12	
				ITG	12	4	Mixed	Naïve	GRZ/EBR	12	
DTG	6	4	Mixed	Naïve	GRZ/EBR	12					
Sofosbuvir plus peginterferon plus ribavirin											
NEUTRINO	327	OL, MC, single arm, Phase III	NA	-	327	1, 4-6	Mixed	Naïve	SOF+PR	12	SVR12
Gt 4 subgp	28			-	28	4	Mixed	Naïve	SOF+PR	12	
Cirrhosis subgp	54			-	54	1, 4-6	Yes	Naïve	SOF+PR	12	
Wehmeyer 2015 ^d	87	MC, Cohort	NA	1	24	4	Mixed	Naïve or experienced ^c	SOF +PR	12	SVR12

Note: Technivie® represents treatment with paritaprevir/ritonavir/ombitasvir. Treatment experienced patients include those who have failed peginterferon plus ribavirin. Shaded cells represent the treatment arms that are included in the naïve indirect comparisons.

Abbreviations: CO = crossover; D=delayed treatment group, DB = double-blind; DTG = deferred treatment group; EBR = elbasvir; GRZ = grazoprevir; Gt = genotype; HCV = hepatitis C virus; HIV = human immunodeficiency virus; ITG = immediate treatment group; MC = multi-centre; NA = not applicable; OL = open-label; PBO = placebo; PR = peginterferon plus ribavirin; R = randomised; RBV=ribavirin; Tx = treatment; SOF = sofosbuvir; subgp = subgroup; SVR12 = sustained virological response at 12 weeks following the completion of treatment

^a all studies had excluded patients with decompensated cirrhosis (no information for Wehmeyer 2015 study)

^b 100 randomised to placebo, 95 received deferred GRZ-EBR treatment

^c failed peginterferon plus ribavirin was not defined in Wehmeyer 2015

^d indicates results extracted during the evaluation

Source: constructed during the evaluation.

- 6.7 There was no common comparator across the studies; overall the evaluation of efficacy in GT4 CHC was based on the results of single arms of the included studies using unadjusted indirect comparisons.
- 6.8 The risk of bias associated with comparisons of Technivie® + RBV against active comparators (GRZ-EBR ± RBV and SOF + PR) was considered high by the evaluation. This was because despite being an objective outcome, sustained virologic response (SVR) is affected by differences in baseline patient characteristics and other clinical parameters. Even in apparently similar populations, the magnitude of any difference in SVR rates between trials is not only related to the treatments administered but also known and unknown confounders. Therefore, in the absence of a common comparator arm, exchangeability between trials/studies cannot be ascertained. The comparison was made even more difficult as the submission further relied on subgroups within the single arms of some studies. GT4 patients were a minority (as low as 6%) in some studies, and the reporting of baseline characteristics and efficacy outcomes for these patients was limited, making the assessment of exchangeability impossible. The ESC considered the trial populations for Technivie® + RBV and GRZ-EBR ± RBV reasonably comparable in terms of HCV RNA at baseline and noted that the exchangeability of such studies may be further informed by comparing viral load of the study populations.
- 6.9 The Pre-PBAC Response (p2) presented a comparison of baseline viral load in treatment arms for Technivie® trials vs GZR-EBR trials (where information was available). The Pre-PBAC Response stated that it was difficult to draw conclusions from such data, but noted that mean HCV RNA values at baseline were in a similar numerical range.
- 6.10 A majority of the included studies were open-label. Although this is not expected to generate bias in the assessment of virologic response, as it is measured using an objective test, there is risk of bias in the attribution of the causation of adverse events (AEs) and in the grading of the severity of AEs.

Comparative effectiveness

- 6.11 Table 3 summarises the SVR rates measured at 12 weeks after the end of treatment (SVR12) observed in patients treated with Technivie® + RBV and GZR-EBR ± RBV.

Table 3: Comparison of SVR12 rates (n/N (%) [95% CI]): Technivie® +RBV12 versus GZR-EBR 12 and GZR-EBR + RBV16

Treatment naïve									
	Technivie® + RBV12				GZR-EBR12				
	PEARL I	AGATE I	AGATE II		C-EDGE TN	C-EDGE CO-INF	C-SCAPE	C-EDGE CO-STAR ^d	
	Group 4 (TN, no cirr)	Arm A (TN, cirr)	Arm A (TN 49%, no cirr)	Arm B (TN 48%, cirr)	ITG (TN, no cirr & cirr)	(TN, no cirr & cirr)	Arm B3 (TN, no cirr & cirr)	ITG (TN, no cirr & cirr)	DTG (TN, no cirr & cirr)
All HCV Gt 4 patients	42/42 (100) [91.6, 100] ^a	29/30 (96.7) [82.8, 99.9]	94/100 (94.0) [87.4, 97.8]	30/31 (96.8) [83.3, 99.9]	18/18 (100) [81.5, 100] ^a	27/28 (96.4) [81.7, 99.9]	9/10 (90.0) [55.5, 99.7]	11/12 (91.7) [61.5, 99.8]	6/6 (100) [54.1, 100] ^a
Pooled	195/203 (96.1) [92.4, 98.3] ^b				71/74 (95.9) [88.6, 99.2]				
Diff in %	p=0.966								
Treatment experienced									
	Technivie® + RBV12				GZR-EBR + RBV16				
	PEARL I	AGATE I	AGATE II		C-EDGE TE				
	Group 6 (TE, no cirr)	Arm A (TE, cirr)	Arm A (TE 51%, no cirr)	Arm B (TE 52%, cirr)	Arm D (TE, no cirr & cirr)				
All HCV Gt 4 patients	49/49 (100) [92.7, 100] ^a	28/29 (96.6) [82.2, 99.9]	94/100 (94.0) [87.4, 97.8]	30/31 (96.8) [83.3, 99.9]	8/8 (100.0) [63.1, 100] ^a				
Pooled	201/209 (96.2) [92.6, 98.3] ^c				8/8 (100.0) [63.1, 100] ^a				
Diff in %	p=0.573								

Abbreviations: CI = confidence interval; cirr = cirrhosis; diff= difference; DTG = delayed treatment group (received placebo initially); EBR = elbasvir; Gt = genotype; GZR = grazoprevir; HCV = hepatitis C virus; ITG = immediate treatment group; RBV = ribavirin; RBV12/16=ribavirin administered for 12 weeks or 16 weeks, SVR12 = sustained virological response at 12 weeks following the completion of treatment; TE = treatment experienced; TN = treatment naïve

Note: Technivie® represents treatment with paritaprevir/ritonavir/ombitasvir. Results for C-EDGE CO-STAR from Dore *et al* (2016) were incorporated during the evaluation in the same method as the other indirect comparisons presented in the submission for consistency (i.e. the identified subgroups/single arms were combined ('lumped'), then the exact binomial 95% CI were calculated. The p-values were based on the Chi-squared test).

^a one sided 97.5% CI as the point estimate is 100, already the maximum of the possible range

^b 67% of this pooled population was treatment naïve, the rest were treatment experienced.

^c 69% of this pooled population was treatment experienced, the rest were treatment naïve.

^d the results for C-EDGE CO-STAR were identified and incorporated during the evaluation.

Source: Tables B-35, p152 and B-36, p153 of the submission; Dore *et al* (2016)

- 6.12 SVR12 response rates were high for all treatments irrespective of patients' prior treatment history (range: 90% to 100%).
- 6.13 During the evaluation, it was noted that despite labelling results of the AGATE II trial 'treatment naïve' and 'treatment experienced', the results reported for both groups were identical and included a mixture of treatment experienced and naïve patients. This is because the poster presentation for AGATE II (Waked 2016) did not present results by treatment history. Therefore, in the pooled populations for Technivie® + RBV, only 67% of the 203 and 69% of the 209 patients were actually treatment naïve and treatment experienced, respectively.
- 6.14 For 'treatment naïve' patients, the submission estimated that the SVR12 rate for Technivie® + RBV was 96.1% (95% CI: 92.4%, 98.3%) and the evaluation adjusted

SVR12 rate for GZR-EBR was 95.9% (95%: CI 88.6%, 99.2%), incorporating results from C-EDGE CO-STAR, identified during the evaluation. For 'treatment experienced' patients, the estimated SVR12 rates were 96.2% (95% CI: 92.6%, 98.3%) and 100% (95% CI: 63.1%, 100%) for Technivie® + RBV and GZR-EBR + RBV 16 weeks, respectively. The confidence intervals of the comparisons are largely overlapping and for GZR-EBR ± RBV, the estimated 95% CIs were wide due to smaller numbers of patients. Due to differences across studies and uncertainty due to lack of exchangeability, these results need to be interpreted with caution.

- 6.15 Table 4 compares the SVR12 rates observed in patients treated with Technivie® + RBV versus SOF + PR.

Table 4: Comparison of SVR12 rates (n/N (%) [95% CI]): Technivie® + RBV12 versus SOF + PR12

	Technivie® + RBV12					SOF + PR12	
	PEARL I		AGATE I	AGATE II		NEUTRINO	Wehmeyer 2015 ^b
	Group 4 (TN, no cirr)	Group 6 (TE, no cirr)	Arm A (TN&TE, cirr)	Arm A (TN&TE, no cirr)	Arm B (TN&TE, cirr)	(TN, no cirr & cirr)	(TN&TE, no cirr & cirr)
All HCV GT 4 patients	42/42 (100.0) [91.6, 100] ^a	49/49 (100.0) [92.7, 100] ^a	57/59 (96.6) [88.3, 99.6]	94/100 (94.0) [87.4, 97.8]	30/31 (96.8) [83.3, 99.9]	27/28 (96.4) [81.7, 99.9]	20/24 (83.3) [62.6, 95.3]
Pooled	272/281 (96.8) [94.0, 98.5]					47/52 (90.4) [79.0, 96.8]	
Diff in %	p=0.03						
	PEARL I		AGATE I	AGATE II		NEUTRINO	Wehmeyer 2015
	-	-	Arm A (TN&TE, GT 4)	-	Arm B (TN&TE, GT 4)	(TN, GT 1, 4, 5, 6)	(likely TN&TE, GT 4)
Cirrhotic patients	-	-	57/59 (96.6) [88.3, 99.6]	-	30/31 (96.8) [83.3, 99.9]	43/54 (79.6) [66.5, 89.4]	4/5 (80.0) [28.4, 99.5]
Pooled	-	-	87/90 (96.7) [90.6, 99.3]			47/59 (79.7) [67.2, 89.0]	
Diff in %	-	-	p<0.001				

Abbreviations: CI = confidence interval; cirr = cirrhosis; diff= difference; Gt = genotype; HCV = hepatitis C virus; PR = peginterferon plus ribavirin; RBV = ribavirin; SOF = sofosbuvir; RBV12=ribavirin for 12 weeks; SOF+PR12= sofosbuvir +peginterferon and ribavirin for 12 weeks SVR12 = sustained virological response at 12 weeks following the completion of treatment; TE = treatment experienced; TN = treatment naïve

Note: Technivie® represents treatment with paritaprevir/ritonavir/ombitasvir. Results from Wehmeyer et al (2015) were incorporated during the evaluation in the same method as the other indirect comparisons presented in the submission for consistency (i.e. the identified subgroups/single arms were combined ('lumped'), then the exact binomial 95% CI were calculated. The p-values were based on the Chi-squared test).

^a one sided 97.5% CI as the point estimate is 100, already the maximum of the possible range

Source: Table B-55, p295 of the submission; Wehmeyer *et al* (2015).

^b the results for Wehmeyer (2015) were identified and incorporated during the evaluation.

- 6.16 SVR12 rates following Technivie® + RBV or SOF + PR treatment in GT4 CHC patients were consistently high (see Table 4). The point estimate of SVR12 in all studies exceeded 90% with the exception of Wehmeyer 2015 (80%), which potentially had patients with more advanced disease as recruitment was from real life clinics.

- 6.17 Due to smaller GT4 CHC patient numbers in the SOF + PR studies, the confidence intervals are wider. The NEUTRINO study did not report outcomes separately for GT4 patients with cirrhosis. Rather, results were reported for a mixed group of GT1,

4, 5 and 6 cirrhotic patients. Based on this population, the proportion of cirrhotic patients attaining SVR12 was higher for Technivie® + RBV versus SOF + PR. From this, the submission contended that Technivie® + RBV was superior to SOF + PR in cirrhotic patients with GT4 CHC and suggested that cirrhosis was strongly associated with a reduced response for SOF + PR but not for Technivie® + RBV. The evaluation considered this claim may not be appropriate, as instead of a true difference in the efficacy of the two treatments, the difference could also be due to:

- chance and/or
- the violation of the exchangeability assumption underpinning the indirect comparison. There was potential for confounding from many factors e.g. non-CC IL28B genotype were strongly associated with a reduced response as per NEUTRINO study publication, other factors (as per the PI) also include high baseline viral concentrations, black race, prior null response to peginterferon alfa and ribavirin therapy. The distribution of known and unknown confounding factors between the single arms/subgroups is unclear.

Due to differences across studies and uncertainty due to lack of exchangeability, these results need to be interpreted with caution.

Comparative harms

- 6.18 The most commonly observed AEs across all the studies for Technivie® and comparators were fatigue, asthenia and headache. The rates of anaemia were higher in cirrhotic compared to non-cirrhotic patients.
- 6.19 For Technivie® there were safety data for 415 GT4 CHC patients, of which 180 patients had compensated cirrhosis and 235 patients were non-cirrhotic. In summary:
- Approximately 80% of the patients in the Technivie® trials experienced at least one treatment related adverse event; the most commonly observed AEs were headache, asthenia, nausea and fatigue.
 - Grade 3/4 AEs (serious adverse events; SAEs) were observed in 11 out of 415 (3%) patients treated with Technivie® of which only 5 (1.2%) were considered related to Technivie® or RBV. None of the subjects discontinued treatment due to AEs.
 - There was one death across the Technivie® trials, which was due to cardiac arrest caused by self-administered suxamethonium to treat leg muscle cramping. Suxamethonium is not listed as a drug interaction for Technivie® based on its draft PI. The submission stated the death was not considered related to Technivie® treatment.
- 6.20 When compared to GZR-EBR ± RBV, a similar proportion of patients treated with Technivie® and GZR-EBR ± RBV experienced at least one adverse event and serious adverse event. No patients discontinued treatment due to an AE in the Technivie® treatment arms compared to 1.2% of patients in the GZR-EBR ± RBV treatment arms. RBV treatment is associated with its own AEs, particularly anaemia. Therefore, for treatment naïve patients, GZR-EBR treatment may be associated with fewer side effects compared to Technivie® + RBV, as RBV is not required to be co-administered.
- 6.21 Compared to SOF + PR, fewer patients treated with Technivie® + RBV experienced AEs, i.e. 80 to 88% compared with 95% of patients treated with SOF + PR in NEUTRINO, results were not available for Wehmeyer 2015. The rate of SAE was slightly higher in AGATE I (6.7%) and AGATE II (2%) compared to NEUTRINO

(1.2%), but was lower in PEARL I (<1%). There were more treatment discontinuations in NEUTRINO (2.4%). A higher proportion of patients also required drug dose modifications due to AEs in the SOF + PR studies [109 (33.3%) in NEUTRINO, and not reported in Wehmeyer 2015] compared to the Technivie® trials (6%-25% across PEARL I, AGATE I and II). No deaths were reported in the SOF + PR studies. Hematologic toxicities (anaemia and thrombocytopenia), influenza-like symptoms, gastrointestinal disorders, drug-induced rash events, and psychiatric events generally occurred at a numerically higher frequency in patients treated with SOF + PR compared with patients treated with Technivie® + RBV.

- 6.22 Post-marketing reports of hepatic decompensation and/or failure including liver transplantation or death associated with the 3-DAA (Viekira®) and 2-DAA (Technivie®) regimens were identified. Most patients with severe events had evidence of advanced or decompensated cirrhosis prior to initiating therapy. To investigate, the United States Food and Drug Administration (US FDA) requested a cumulative review of reports of hepatic failure and hepatic decompensation including an independent assessment by an External Hepatic Panel (EHP). As a result of the review, in October 2015: the US FDA [REDACTED]. The Company Core Data Sheet (CCDS) was also updated to include a warning of post-marketing events of hepatic decompensation, a statement that the 3-DAA (Viekira®) and 2-DAA regimens (Technivie®) are not recommended in patients with Child-Pugh B cirrhosis and monitoring instructions for cirrhotic patients. The US FDA also required the insertion of a new contraindication for patients with Child-Pugh B cirrhosis (a change from the previous wording of 'not recommended' in Child-Pugh B patients). A Dear Health Care Provider (DHCP) letter was sent out by the sponsor to prescribers in the US, EU and Brazil to inform them of the change in the Product Information (PI).
- 6.23 The PSCR (p2) provided an updated draft Technivie® PI (dated 13 September 2016), which indicates use of Technivie® is not recommended in patients with moderate hepatic impairment (Child-Pugh B) and is contraindicated in patients with severe hepatic impairment (Child-Pugh C).
- 6.24 Based on the cumulative review of post-marketing reports, reports of decompensation and liver failure were not limited to patients with Child-Pugh B and C cirrhosis but also included patients with no evidence of cirrhosis or with only mild cirrhosis (Child-Pugh A), although at a lower incidence. It was noted that for some patients, the outcome of decompensation and failure was severe including liver transplantation and/or death (see approved Product Information for more detail).

- [REDACTED]
- 6.25 The PSCR (pp2-3) outlined factors that it viewed should be considered when assessing the causality of cases of hepatic decompensation in compensated cirrhotic patients reported as post-marketing adverse events, including:

- Confounding by concurrent medical conditions such as extrahepatic infectious processes, cholecystitis, and choledocholithiasis. The PSCR advised that in the majority of AE reports, there was insufficient information to enable causality assessment and there was an absence of information about the status of patients' hepatic disease at baseline.
- Difficulty in ruling out decompensation in patients with cirrhosis occurring as part of the natural history of the disease for a patient with limited hepatic reserves. Natural history of progression to decompensated cirrhosis, as part of the underlying disease state, has been described in several large studies of cirrhotic patients, including patients with Child-Pugh A cirrhosis (Alazawi W et al 2010 & D'Amico G et al 2006).

Benefits/harms

6.26 A summary table of benefits and harms cannot be formulated, given:

- the lack of comparative evidence from head-to-head trials;
- concerns regarding unadjusted indirect comparisons of clinical studies with potential exchangeability issues; and
- the lack of statistically significant differences in SVR rates between Technivie® + RBV therapies and the active comparators.

Clinical claim

6.27 Table 5 summarises the clinical claims made in the submission on the comparative efficacy and safety of Technivie® + RBV for 12 weeks versus the nominated comparators for GT4 CHC.

Table 5: Summary of the clinical claims made in the submission of Technivie® + RBV (12 weeks) versus the nominated comparators for genotype 4 CHC

Comparator	Patient population	Clinical claim		Comment from the evaluation
		Efficacy	Safety	
No Treatment	All GT4 patients	Superior	Inferior	Adequately supported.
GZR-EBR ± RBV	All GT4 patients	Non-inferior	Non-inferior	The clinical claims may be reasonable despite not being adequately supported. A naïve comparison for SVR12 was presented, which had major limitations and was at high risk of bias. For the subgroup of treatment naïve patients not requiring concomitant treatment with RBV, these patients are likely to have fewer RBV associated AEs, particularly anaemia. As both treatments are relatively new, longer term safety with the treatments cannot be compared. There are however already some post-marketing safety concerns for Technivie® with respect to hepatic decompensation and failure which included severe outcomes such as liver transplantation and death.
SOF+PR	Non-cirrhotic GT4 patients	Non-Inferior	Superior	The clinical claims for efficacy and safety may be reasonable despite not being adequately supported.
	Cirrhotic GT4 patients	Superior	Superior	The clinical claim with respect to efficacy is not reasonable and was not adequately supported with the data. A naïve comparison for SVR12 was presented, which had major limitations and was at high risk of bias. The claim with respect to safety, although inadequately supported appear to be reasonable given the well-known limitation associated with peginterferon therapy.

Abbreviations: FDC = fixed-dose combination; GT = genotype; HCV = hepatitis C virus; SOF+PR = sofosbuvir, peginterferon alfa-2a and ribavirin; SVR12 = sustained virological response at 12 weeks following the completion of treatment

Note: Technivie® represents treatment with paritaprevir/ritonavir/ombitasvir

Source: Adapted from pp167-172 of the submission

- 6.28 The PBAC considered that the claim of superior comparative effectiveness and inferior safety in comparison with ‘no treatment’ was reasonable.
- 6.29 The PBAC considered that the claim of non-inferior comparative effectiveness and safety in comparison with GZR-EBR ± RBV was reasonable, despite the limitations in the data set. The PBAC acknowledged that the subgroup of patients who do not require RBV would have fewer RBV associated AEs.
- 6.30 The PBAC considered that the claim of non-inferior comparative effectiveness and superior safety in comparison with SOF+PR for *non-cirrhotic* GT4 patients was reasonable, despite the limitations in the data set.
- 6.31 For *cirrhotic* GT4 patients, the PBAC considered that the claim of superior comparative safety over SOF + PR may be reasonable given the well-known limitations of interferon-containing regimens, but that the claim of superior comparative efficacy over SOF + PR was not reasonable, with insufficient data to support the claim.

Economic analysis

- 6.32 Although an economic analysis was presented (a modelled cost-utility analysis versus ‘no treatment’), the submission indicated that the sponsor was willing to accept a price for Technivie® based on a cost-minimisation analysis versus GZR-EBR ± RBV.

Drug cost/patient/course

6.33 \$ [REDACTED] for the full 12 weeks of treatment based on the proposed effective price.

Estimated PBS usage & financial implications

6.34 This submission was not considered by DUSC. The submission used an epidemiological approach in the estimation of the financial impact of listing Technivie® on the PBS (Table 7).

Table 7: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated extent of use					
Number treated	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Scripts ^a	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Estimated net cost to PBS/RPBS/MBS					
Net cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to MBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Estimated total net cost					
Net cost to PBS/RPBS/MBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

^a Assuming [REDACTED] scripts would be required for 12 week course.

Source: adapted from Table E-12, p260 of the submission; Technivie® Section E Workbook.xlsx.

6.35 With respect to the MBS costs applied, some anomalies with the choice of MBS items and the application of benefit were noted. For example the MBS item selected for ultrasound (MBS: 55854) refers to paediatric spine, spinal cord and over laying subcutaneous tissues, which is not the correct item for a liver ultrasound, however the cost was similar to those quoted for an abdominal ultrasound (item: 55037). Also the benefit that is payable for specialist visits and pathology is usually 85% of the benefit rather than the full amount, however this is unlikely to change the estimates. Thyroid function test (\$34.80) is also not usually required unless patients are taking interferon. One additional HCV RNA quantitative assay may be required for patients with cirrhosis.

6.36 The financial estimates are most sensitive to the assumed uptake rates for Technivie®. A 20% increase or decrease in the assumed uptake rates (base case for Year 1 was [REDACTED], thus assuming a 20% increase or decrease would make the rate [REDACTED] and [REDACTED] respectively), this resulted in a corresponding 14% increase or decrease in the estimated cost to government.

6.37 At year 5, the submission-estimated number of patients was less than 10,000 and the net cost to the PBS was less than \$10 million.

Quality Use of Medicines

6.38 The submission did not present any information in relation to quality use of medicine (QUM). A number of potential QUM issues were considered during the evaluation. Of importance is the minimisation of the risks of liver decompensation / liver failure (particularly in patients with cirrhosis).

6.39 The PSCR (p4) described current medical education initiatives undertaken to reinforce the recommendation not to treat patients with Child-Pugh B and Child-Pugh C with Viekira Pak®/Viekira Pak-RBV® and Technivie®. The PSCR also provided

the Australian annex of the Risk Management Plan submitted to the TGA for Viekira Pak®/Viekira Pak-RBV® and Technivie®, which included measures such as updates to the PI contraindications and precautions, updates to the Consumer Medicine Information to include symptoms of severe liver problems, and routine and targeted pharmacovigilance surveillance.

Financial Management – Risk Sharing Arrangements

- 6.40 None proposed, but the submission proposed an effective DPMQ price for Technivie® of \$██████████ per pack. This is approximately ██████% of its published price.
- 6.41 The PBAC recommended that Technivie® enter the Risk Sharing Arrangement (RSA) currently in place for other drugs used for the treatment of CHC, and be subject to the same Subsidisation Caps and rebate arrangements.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the Authority Required General Schedule and Section 100 listing of paritaprevir with ritonavir and ombitasvir, in combination with ribavirin for treatment naïve and treatment experienced genotype 4 CHC infection on a cost-minimisation basis with grazoprevir with elbasvir with or without RBV, in accordance with the treatment recommendations in the approved Australian Product Information for each product.
- 7.2 The PBAC recommended that the cost of a course of treatment for paritaprevir with ritonavir and ombitasvir + RBV should be the same as the cost of a course of treatment with GZR-EBR ± RBV for patients with GT4 CHC.
- 7.3 The PBAC considered that the PBS restriction should be consistent with other drugs listed in the *General Statement for Drugs for the Treatment of Hepatitis C*, and recommended that the maximum quantity should provide for one pack, and two repeats, allowing for 12 weeks' of treatment. The PBAC also noted that the exact restriction will be finalised following TGA registration of the drug.
- 7.4 In terms of the clinical place for paritaprevir with ritonavir and ombitasvir, in combination with ribavirin, the PBAC viewed that this regimen would provide an additional interferon-free treatment option for patients with GT4 CHC. Currently, these patients have access to PBS-subsidised sofosbuvir in combination with peginterferon and ribavirin. GZR-EBR regimens were recommended for PBS use in this patient population at the July 2016 PBAC meeting. The PBAC noted that GZR-EBR may be contraindicated in some patients who would be able to use paritaprevir with ritonavir and ombitasvir + RBV.
- 7.5 The PBAC considered that the most appropriate comparator was GZR-EBR ± RBV as it is the only interferon-free treatment for GT4 currently recommended for PBS listing, and would therefore be the therapy most likely to be replaced in clinical practice.
- 7.6 The PBAC considered that the clinical evaluation presented by the submission –

based on unadjusted indirect comparisons between single arms of the included studies – was at high risk of bias. In the absence of a common comparator arm, exchangeability between studies cannot be established. The PBAC noted the ESC advice that the trial populations for paritaprevir with ritonavir and ombitasvir + RBV and GRZ-EBR ± RBV were reasonably comparable in terms of HCV RNA at baseline and that the exchangeability of such studies may be further informed by comparing viral load of the study populations. The PBAC also noted the Pre-PBAC Response (p2), which presented a comparison of baseline viral load in treatment arms for paritaprevir with ritonavir and ombitasvir trials vs GZR-EBR trials (where information was available). The Pre-PBAC Response stated that it was difficult to draw conclusions from such data, but noted that mean HCV RNA values at baseline were in a similar numerical range.

- 7.7 Overall, the PBAC agreed that SVR12 response rates were high for all treatments irrespective of patients' prior treatment history. However, the PBAC considered that the claims about comparative benefits between treatments should be interpreted with caution due to the lack of exchangeability between studies. Nevertheless, the PBAC viewed that it was not unreasonable to conclude non-inferior comparative efficacy between paritaprevir with ritonavir and ombitasvir + RBV and GZR-EBR ± RBV. The PBAC considered that there was limited data to support the submission's claim that paritaprevir with ritonavir and ombitasvir + RBV had superior comparative efficacy over SOF + PR.
- 7.8 In terms of comparative harms, the PBAC again considered that the results should be interpreted with caution due to the non-comparative nature of the evidence presented. At the same time, the PBAC considered it reasonable to conclude that paritaprevir with ritonavir and ombitasvir + RBV had:
- inferior safety compared with 'no treatment';
 - non-inferior safety compared with GZR-EBR ± RBV (although acknowledging that the subgroup of patients who do not require RBV would have fewer RBV associated AEs);
 - superior safety compared with SOF + PR, due to the well-known limitations of peginterferon-containing regimens.
- 7.9 Furthermore, the PBAC considered it important to note that there are safety concerns for the use of paritaprevir with ritonavir and ombitasvir + RBV amongst people with advanced liver disease – the use of paritaprevir with ritonavir and ombitasvir is not recommended in patients with moderate hepatic impairment (Child-Pugh B) and is contraindicated in patients with severe hepatic impairment (Child-Pugh C). The PBAC noted that these concerns have been clearly articulated in the draft TGA Product Information, and reflect the TGA cautions in place for Viekira-PAK® and Viekira-PAK®+RBV, which are already listed on the PBS.
- 7.10 The PBAC also recommended that paritaprevir with ritonavir and ombitasvir enter the RSA currently in place for other drugs used for the treatment of CHC, and be subject to the same Subsidisation Caps and rebate arrangements.
- 7.11 The PBAC considered that listing paritaprevir with ritonavir and ombitasvir would only substitute for other DAA-containing treatment regimens for CHC GT4 infection and would not grow the total market.

- 7.12 The PBAC recommended that, under s101(3BA) of the *National Health Act 1953*, paritaprevir with ritonavir and ombitasvir + RBV should be treated as interchangeable on an individual patient basis with grazoprevir with elbasvir ± RBV, for the treatment of patients with GT4 CHC.
- 7.13 The PBAC advised that paritaprevir with ritonavir and ombitasvir should have the same nurse practitioner prescribing arrangements as other HCV treatments under the *General Statement*.
- 7.14 The PBAC recommended that the Early Supply Rule should apply to the listing of paritaprevir with ritonavir and ombitasvir under the General Schedule.
- 7.15 The PBAC noted that this submission was not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing (to be finalised following TGA registration)

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty (units)	Max. Qty (packs)	No. of Rpts	Proprietary Name and Manufacturer	
PARITAPREVIR + RITONAVIR + OMBITASVIR Paritaprevir 75 mg + ritonavir 50 mg + ombitasvir 12.5 mg tablet	56	1	2	Technivie®	AbbVie Pty Ltd
Category / Program:	GENERAL – General Schedule (Code GE) Section 100 – Highly Specialised Drugs Program				
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners (GE listing only)				
PBS Indication:	Chronic hepatitis C infection				
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone				
Clinical criteria:	Patient must meet the criteria set out in the General Statement for Drugs for the Treatment of Hepatitis C, AND Patient must be taking this drug as part of a regimen set out in the matrix in the General Statement for Drugs for the Treatment of Hepatitis C, based on the hepatitis C virus genotype, patient treatment history and cirrhotic status, AND The treatment must be limited to a maximum duration of 12 weeks.				
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.				

Additions to the *General Statement for Drugs for the Treatment of Hepatitis C* will be finalised following TGA registration.

9 Context for Decision

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

10 Sponsor's Comment

AbbVie welcomes the decision of the PBAC.