6.15 GLECAPREVIR with PIBRENTASVIR, Tablet containing 100 mg glecaprevir with 40 mg pibrentasvir, Maviret®, AbbVie Pty Ltd.

1 Purpose of Application

1.1 The minor submission requested that the PBAC consider the reimbursement of glecaprevir with pibrentasvir (GLE-PIB) for a small sub population of patients infected with chronic hepatitis C (CHC) that have failed prior treatment with the use of an NS5A inhibitor. This submission follows from a major submission deferred (pending the outcome of the TGA's considerations) at the July 2017 PBAC meeting for glecaprevir with pibrentasvir, requesting reimbursement for the treatment of patients with genotypes 1-6 hepatitis C virus (HCV) on a cost-minimisation basis to Epclusa (sofosbuvir/velpatasvir).

2 Requested listing

2.1 To be finalised following TGA registration. The proposed amendments to the *General Statement for Drugs for the Treatment of Hepatitis C* are given below. The full proposed restriction is at the end of this document. Additions to the requested listing are added in italics and deletions are crossed out with strikethrough.

2.2 The submission requested that the treatment matrices in the General Statement for Drugs for the Treatment of Hepatitis C include a 16 week treatment regimen of glecaprevir with pibrentasvir for patients who have failed prior treatment with an N5SA inhibitor (also called N5SA treatment experienced patients) as outlined in Table 1 – this change would be given effect through an amendment to the footnote to the general statement. (The submission considered at the July 2017 meeting included treatment regimens of 8-, 12-, or 16-weeks for treatment naïve patients with and without cirrhosis and treatment experienced patients with and without cirrhosis.

Table 1: Treatment Matrix

Treatment Matrix		
Hepatitis C – Non –cirrhotic patients		
	Treatment naïve	**Treatment experienced**
Genotype 1-6	**GLECAPREVIR + PIBRENTASVIR** [8 weeks]	**GLECAPREVIR + PIBRENTASVIR** [8 *or 16 weeks*][a] ~~OR~~ ~~**GLECAPREVIR + PIBRENTASVIR**~~ ~~[16 weeks][a]~~
Hepatitis C –Cirrhotic patients		
	Treatment naïve	**Treatment experienced**
Genotype 1-6	**GLECAPREVIR + PIBRENTASVIR** [12 weeks]	**GLECAPREVIR + PIBRENTASVIR** [12 *or 16 weeks*][a] ~~OR~~ ~~**GLECAPREVIR + PIBRENTASVIR**~~ ~~[16 weeks][a]~~

Notes: [a]~~**for NS5A treatment experienced and all GT3 *[GLECAPREVIR + PIBRENTASVIR] for***~~ **treatment experienced patients *with genotype 3 HCV and patients who have failed an NS5A inhibitor*, treatment is for 16 weeks.**

2.3 Upon TGA approval of glecaprevir with pibrentasvir the sponsor requests a dual listing to ensure all patients with CHC have access to treatment through a:

- General Schedule Authority Required listing, or a
- Section 100 HSD program Authority Required listing.

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

3 Background

3.1 The previous major submission was made under TGA/PBAC Parallel Process. At the time of PBAC consideration for this submission, a positive TGA Delegate's overview had been received.

3.2 This is the second submission requesting PBS-listing of glecaprevir with pibrentasvir. Glecaprevir with pibrentasvir was previously considered by the PBAC in July 2017 for PBS listing of the fixed dose combination (FDC) of glecaprevir with pibrentasvir for the treatment of chronic hepatitis C for genotypes 1-6. At that time, in response to questions raised during the evaluation regarding the appropriateness of sofosbuvir/velpatasvir as a comparator for patients who have failed prior NS5A inhibitors, the sponsor withdrew the request for reimbursement for the small sub-population of patients who have failed prior treatment with an NS5A inhibitor.

3.3 This minor submission requested that the reimbursement of glecaprevir with pibrentasvir for subgroup of patients who have failed prior treatment with an NS5A inhibitor, be considered by the PBAC.

3.4 At its meeting of July 2017, the PBAC was of a mind to recommend the Authority Required General Schedule and Section 100 listings of glecaprevir with pibrentasvir for the treatment of chronic hepatitis C infection (CHC) for treatment naïve and treatment experienced patients with genotypes 1-6, with or without cirrhosis. However, the PBAC deferred making a final recommendation pending the provision of the relevant TGA delegate's overview.

3.5 The TGA delegate's overview was received prior to the November PBAC meeting.

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

4 Population and disease

4.1 Hepatitis C is a blood-borne inflammatory liver disease caused by hepatitis C virus (HCV), with around 75-80% of people exposed to HCV developing chronic infection which may lead to cirrhosis, liver failure, hepatocellular carcinoma and death. Approximately 230,000 people in Australia were estimated to be living with chronic HCV infection in 2014 (Kirby 2015).

4.2 The glecaprevir with pibrentasvir FDC is an alternative treatment option to hepatitis C antivirals already listed on the PBS for the treatment of this condition. Glecaprevir is a HCV NS3/4A protease inhibitor. HCV NS3/4A protease is necessary for the creation of proteins essential for viral replication. Pibrentasvir is a HCV NS5A protein inhibitor. HCV NS5A protein is essential for viral RNA replication and virion assembly.

5 Comparator

5.1 The minor submission nominated no treatment as the comparator in NS5A experienced patients. The PBAC considered that this was the appropriate comparator.

5.2 The previous major submission considered by the PBAC in July 2017 nominated sofosbuvir/velpatasvir as the main comparator. This was considered the appropriate comparator for non NS5A experienced patients.

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 as it was a minor submission.

Consumer comments

6.2 The PBAC noted and welcomed the input received from professional organisations representing people living with hepatitis (4) via the consumer comments facility on the PBS website. The comments described a range of benefits of treatment with glecaprevir/pibrentasvir including the addition of another pan-genotypic treatment choice for patients with HCV; and that it appears to be efficacious for people with severe chronic kidney disease and compensated cirrhosis. In particular it was noted that glecaprevir/pibrentasvir appears to be efficacious for patients who have received prior antiviral treatment experience – thus providing another treatment option for those patients who have previously been treated for HCV but not cured. The PBAC noted that this input was supportive of the evidence provided in the submission.

Clinical trials

6.3 No new data were presented in the minor submission. The submission referenced the MAGELLAN-1 clinical trial presented in the major submission (see Table 2):

Table 2: Trials and associated reports presented in the re-submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Direct randomised trial(s)		
MAGELLAN-1 (M15-410)	Internal study report: Trial report M15-410. A Randomised, Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Co-Administration of ABT-493 and ABT-530 (or ABT-493/ABT-530) With and Without Ribavirin in Adults With Chronic Hepatitis C Virus (HCV) Infection Who Failed a Prior Direct-Acting Antiviral Agent (DAA)-Containing Therapy	Date of report: 30/11/2016

Source: Public Summary Document – July 2017 PBAC

6.4 The current submission referenced data from Arm E of the MAGELLAN study presented in the July 2017 major submission to support of the efficacy of glecaprevir with pibrentasvir in NS5A experienced patients (see Table 3):

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population			Intervention	Key outcome
				HCV Gt	Cirrhosis	Tx history		
Studies for glecaprevir/pibrentasvir								
MAGELLAN-I	47	R, OL, MC 24 weeks	Low	1,4[a]	Non-cirrhotic & compensated cirrhosis	Tx experienced (who failed a prior DAA)	GLE/PIB16	SVR12

Gt = genotype; MC = multi-centre; OL = open-label; R = randomised; Tx = treatment;
SVR12 = sustained virological response at 12 weeks following the completion of treatment
Source: Public Summary Document – July 2017 PBAC

6.5 The MAGELLAN study recruited GT1 and GT4 DAA experienced patients. The SVR12 rate for Arm E of MAGELLAN-1 was 91.5% [95% CI 79.6, 97.6], based on 44 patients with genotype 1 and three patients with genotype 4 HCV who had had prior treatment with a

direct acting antiviral regimen for HCV (including 34 patients who were NS5A experienced and 13 patients who were PI experienced). The SVR 12 rate by prior treatment experience as reported in the submission is reproduced in Table 4 below.

Table 4: SVR12 rate by prior treatment experience for patients in study MAGELLAN-1 Arm E

Treatment with prior DAA regimen class	SVR12 n/N (%)
NS5A naïve and PI experienced	13/13 (100)[1]
NS5A experienced	30/34 (88.2)
NS5A and PI experienced	13/16 (81.3)
NS5A and PI naïve	17/18 (94.4)

6.6 [redacted] patients experienced virologic failure in the relevant arm (Arm E, 16 weeks duration of treatment) in MAGELLAN-1. All [redacted] patients were NS5A inhibitor experienced and three were experienced with both an NS5A inhibitor and an NS3/4A protease inhibitor. [redacted] patients were IL28B genotype CT or TT, and the [redacted] was not determined. All failed patients had baseline polymorphisms in NS5A. [redacted] patients had cirrhosis. Prior failure of treatment with an NS5A inhibitor may have selected patients with poor prognostic features (such as IL28B non-CC, cirrhosis and NS5A resistant polymorphisms).

6.7 In Arm E of MAGELLAN-1, 94% of patients had genotype 1. The clinical efficacy of glecaprevir with pibrentasvir in patients who have genotypes other than 1 is largely unknown. The submission relies on in-vitro data to extrapolate the results in GT1 and 4 patients to patients with other genotypes.

6.8 On the basis of these data the submission claimed that glecaprevir with pibrentasvir is effective in NS5A experienced patients.

Clinical claim

6.9 The minor submission did not make a separate clinical claim for patients who have failed prior treatment with an NS5A inhibitor. The July 2017 major submission described glecaprevir/pibrentasvir as equivalent in terms of efficacy and safety compared with sofosbuvir/velpatasvir in subjects across all CHC genotypes.

6.10 Based on the evidence provided in the minor submission the PBAC considered that glecaprevir/pibrentasvir has superior efficacy and inferior safety when compared to no treatment; and is non-inferior in efficacy and safety when compared to other current listed DAA for chronic hepatitis across all CHC genotypes for patients who are NS5A treatment experienced.

Economic analysis

6.11 The current submission states the paritaprevir, ritonavir and ombitasvir (Technivie®) model has previously been evaluated (November 2016 PBAC meeting) and has been used in the current submission to demonstrate that glecaprevir with pibrentasvir is cost-effective in patients who have failed an NS5A inhibitor. Although this submission relies

on the economic model provided in the PBAC submission for Technivie® to support its claim that glecaprevir with pibrentasvir is cost-effective in NS5A treatment experienced patients, the PBAC recommendation for Technivie® was made on a cost-minimisation basis with grazoprevir with elbasvir (Zepatier®, MSD). In other words, the PBAC has not previously accepted the Abbvie model as a basis for assessing the cost-effectiveness of chronic hepatitis C treatments.

6.12 However, the current submission requests the same price per course for glecaprevir with pibrentasvir in NS5A treatment experienced patients as for glecaprevir with pibrentasvir in other genotypes, and as for sofosbuvir with velpatasvir (Epclusa®, Gilead).

6.13 In the previous major submission considered by PBAC in July 2017, the submission also presented a cost-minimisation analysis against sofosbuvir/velpatasvir.

6.14 The major submission of July 2017 proposed an indicative effective price of $[redacted] per patient per course, based on the published price of sofosbuvir/velpatasvir. The minor submission requested the price of glecaprevir with pibrentasvir per patient per course for the NS5A experienced population be the same as that for NS5A naïve patients and proposed an effective price of $[redacted] for 16 weeks of therapy.

Estimated PBS usage & financial implications

6.15 The current restrictions for the DAA for chronic hepatitis C do not preclude retreatment for patients who have failed to respond to the first DAA regimen used. The PBAC reiterated its recommendation, from the consideration of the major submission in July 2017, that glecaprevir/pibrentasvir 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. The PBAC considered that the listing of glecaprevir/pibrentasvir for NS5A experienced patients will not increase the cost to the Government as these patients can be treated under the current listings.

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

7 PBAC Outcome

7.1 The PBAC, recalling it had deferred the major submission from July 2017 pending the provision of the relevant TGA delegate's overview - which has now been received, recommended the Authority Required General Schedule and Section 100 listing of glecaprevir with pibrentasvir for the treatment of chronic hepatitis C infection for treatment naïve and treatment experienced patients (including those with prior NS5A treatment) with genotypes 1-6, with or without cirrhosis.

7.2 The PBAC reiterated its July 2017 advice that the PBS restriction should be consistent with other DAA drugs listed in the General Statement for Drugs for the Treatment of Hepatitis C (*General Statement*) and that the exact restriction wording would need to be

finalised following TGA registration of the drug. The PBAC considered the addition of a footnote in the *General Statement* to be appropriate for NS5A treatment experienced patients requiring treatment for 16 weeks. For NS5A treatment naïve patients the PBAC reiterated that the maximum quantity should provide for one pack, and three repeats, allowing for up to 16 weeks treatment duration.

7.3 Based on the evidence provided in the minor submission, the PBAC considered that glecaprevir with pibrentasvir has superior efficacy and inferior safety when compared to no treatment; and is non-inferior in efficacy and safety when compared to other current listed DAA for chronic hepatitis across all CHC genotypes for patients who are NS5A treatment experienced.

7.4 The PBAC considered that the request for the same price per course for glecaprevir with pibrentasvir in NS5A treatment experienced patients as for glecaprevir with pibrentasvir in other genotypes was reasonable. The PBAC noted the previous major submission from July 2017 presented a cost-minimisation analysis against sofosbuvir with velpatasvir with a proxy price of $[redacted] per course. At that time the PBAC accepted that cost-minimisation against sofosbuvir with velpatasvir was appropriate and noted that final cost-minimisation calculations would need to be undertaken once the TGA recommended dosing regimens for each of the sub-populations are known.

7.5 The PBAC recalled that the availability of this regimen would likely have a considerable impact on prescribing choices for HCV treatment in Australia. However, the committee considered that the listing of glecaprevir with pibrentasvir will not increase the cost to the Government as the patients that will be treated with this regimen can be treated under the current listings and the costs incurred by these patients will therefore be managed by the existing market subsidisation caps.

7.6 The PBAC recommended that, under s101(3BA) of the *National Health Act 1953,* glecaprevir with pibrentasvir should be treated as interchangeable on an individual patient basis with sofosbuvir with velpatasvir and, by extension, the other medicines that PBAC considered interchangeable with sofosbuvir with velpatasvir at its November 2016 meeting.

7.7 The PBAC recommended that glecaprevir with pibrentasvir should have the same nurse practitioner prescribing arrangements as other HCV treatments listed under the *General Statement*. Currently HCV treatments under the *General Statement* are listed for prescribing by authorised nurse practitioners under the General Schedule only. Medicines for the treatment of hepatitis C are not listed for prescribing by authorised nurse practitioners under the S100 Highly Specialised Drugs Program.

7.8 The PBAC recommended that the Early Supply Rule should apply.

Outcome:

Recommended

8 Recommended listing

8.1 Add new item:

Additions to the requested listing are added in italics and deletions are crossed out with strikethrough. The restriction, including additions to the *General Statement for Drugs for the Treatment of Hepatitis C* will be finalised following TGA registration.

Name, Restriction, Manner of administration and form	Max qty packs	Max qty units	№.of Rpts	Proprietary Name and Manufacturer	
GLECAPREVIR/PIBRENTASVIR Tablet 100 mg/40 mg, 84	1	84	3	Maviret®	AbbVie Pty Ltd

Category/ Program	GENERAL – General Schedule (Code GE)
Prescriber type	☐ Dental ☒ Medical Practitioners ☒ Nurse practitioners ☐ Optometrists ☐ Midwives
Severity:	Chronic
Condition:	~~HCV~~ *Hepatitis C* infection
PBS Indication:	Chronic ~~HCV~~ *Hepatitis C* infection
Restriction:	☐ Restricted benefit ☐ Authority Required - In Writing ☒ Authority Required - Telephone ☐ Authority Required – Emergency ☒ Authority Required - Electronic ☐ Streamlined
~~Treatment criteria:~~	~~Must be treated by a medical practitioner 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.~~
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 16 weeks.
~~Population criteria:~~	~~Patient must be aged 18 years or older.~~
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.*

Name, Restriction, Manner of administration and form	Max qty packs	Max qty units	№.of Rpts	Proprietary Name and Manufacturer	
GLECAPREVIR/PIBRENTASVIR Tablet 100 mg/40 mg, 84	1	84	3	Maviret®	AbbVie Pty Ltd

Category/ Program	Section 100 – Highly Specialised Drugs Program
Prescriber type	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
Severity:	Chronic
Condition:	~~HCV~~ *Hepatitis C* infection
PBS Indication:	Chronic ~~HCV~~ *Hepatitis C* infection
Restriction:	☐ Restricted benefit ☐ Authority Required - In Writing ☒ Authority Required - Telephone ☐ Authority Required – Emergency ☒ Authority Required - Electronic ☐ Streamlined
~~**Treatment criteria:**~~	~~Must be treated by a medical practitioner 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.~~
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 16 weeks.
~~**Population criteria:**~~	~~Patient must be aged 18 years or older.~~
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.*

General Statement for Drugs for the Treatment of Hepatitis C

Use the following criteria to determine patient eligibility for subsidisation under the PBS for hepatitis C treating agents.

By writing a PBS prescription, the prescriber is certifying the patient satisfies the qualifying criteria set out below and the use in accordance with the registered indications which differ between agents in this class – refer to the current Product Information for details.

Population criteria: Patient must be aged 18 years or older.
Treatment criteria: Must be treated by a medical practitioner or an authorised nurse practitioner[1] 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.
The following information must be provided at the time of application: a) the hepatitis C virus genotype; and b) the patient's cirrhotic status (non-cirrhotic or cirrhotic) The following information must be documented in the patient's medical records: 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

The following matrices identify the regimens which are available for PBS prescription for eligible patients, based on the hepatitis C virus genotype and treatment history.

Hepatitis C - Non-cirrhotic patients

	Treatment naïve	Treatment experienced
Genotype 1	**LEDIPASVIR + SOFOSBUVIR** [8 or 12 weeks] [2] OR **DACLATASVIR** and **SOFOSBUVIR** [12 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks]	**LEDIPASVIR + SOFOSBUVIR** [12 weeks] OR **DACLATASVIR** and **SOFOSBUVIR** [12 or 24 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks]

	Treatment naïve	Treatment experienced
	OR **PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR** [12 weeks] [3] OR **PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR (&) RBV** [12 weeks] [4] OR **GRAZOPREVIR + ELBASVIR** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] OR ***GLECAPREVIR + PIBRENTASVIR*** *[8 weeks]*	OR **PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR** [12 weeks] [3] OR **PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR (&) RBV** [12 weeks] [4] OR **GRAZOPREVIR + ELBASVIR** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** and **RBV** [16 weeks] [5] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[8 or 16 weeks][6]*
Genotype 2	**SOFOSBUVIR** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks]	**SOFOSBUVIR** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks]

	Treatment naïve	Treatment experienced
	OR ***GLECAPREVIR + PIBRENTASVIR*** *[8 weeks]*	*OR* ***GLECAPREVIR + PIBRENTASVIR*** *[8 or 16 weeks][6]*
Genotype 3	**DACLATASVIR** and **SOFOSBUVIR** [12 weeks] OR **SOFOSBUVIR** and **RBV** [24 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] OR ***GLECAPREVIR + PIBRENTASVIR*** *[8 weeks]*	**DACLATASVIR** and **SOFOSBUVIR** [12 weeks] OR **SOFOSBUVIR** and **RBV** [24 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[8 or 16 weeks][6]*
Genotype 4	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** [12 weeks]	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** [12 weeks]

	Treatment naïve	Treatment experienced
	OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] OR ***GLECAPREVIR + PIBRENTASVIR*** *[8 weeks]*	OR **GRAZOPREVIR + ELBASVIR** and **RBV** [16 weeks] [5] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[8 or 16 weeks][6]*
Genotype 5 & 6	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] OR ***GLECAPREVIR + PIBRENTASVIR*** *[8 weeks]*	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[8 or 16 weeks][6]*

KEY

- PEG-IFN- peginterferon alfa-2a
- RBV - ribavirin

Hepatitis C – Cirrhotic patients

	Treatment naïve	Treatment experienced
Genotype 1	**LEDIPASVIR + SOFOSBUVIR** [12 weeks] OR **DACLATASVIR** and **SOFOSBUVIR** and **RBV** [12 weeks] OR **DACLATASVIR** and **SOFOSBUVIR** [24 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR (&) RBV** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 weeks]*	**LEDIPASVIR + SOFOSBUVIR** [24 weeks] OR **DACLATASVIR** and **SOFOSBUVIR** [24 weeks] OR **DACLATASVIR** and **SOFOSBUVIR** and **RBV** [12 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR (&) RBV** [12 or 24 weeks] [8] OR **GRAZOPREVIR + ELBASVIR** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** and **RBV** [16 weeks] [5] OR **SOFOSBUVIR + VELPATASVIR**

	Treatment naïve	Treatment experienced
		[12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 or 16 weeks][6]*
Genotype 2	**SOFOSBUVIR** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 weeks]*	**SOFOSBUVIR** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 or 16 weeks][6]*
Genotype 3	**SOFOSBUVIR** and **RBV** [24 weeks] OR **DACLATASVIR** and **SOFOSBUVIR** [24 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR	**DACLATASVIR** and **SOFOSBUVIR** [24 weeks] OR **SOFOSBUVIR** and **RBV** [24 weeks] OR **SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR

	Treatment naïve	Treatment experienced
	DACLATASVIR and **SOFOSBUVIR** and **RBV** [12 or 24 weeks] [9] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7][10] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 weeks]*	**DACLATASVIR** and **SOFOSBUVIR** and **RBV** [12 or 24 weeks] [9] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7][10] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 or 16 weeks][6]*
Genotype 4	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 weeks]*	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** [12 weeks] OR **GRAZOPREVIR + ELBASVIR** and **RBV** [16 weeks] [5] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 or 16 weeks][6]*

	Treatment naïve	Treatment experienced
Genotype 5 & 6	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 weeks]*	**SOFOSBUVIR** and **PEG-IFN** and **RBV** [12 weeks] OR **SOFOSBUVIR + VELPATASVIR** [12 weeks][7] *OR* ***GLECAPREVIR + PIBRENTASVIR*** *[12 or 16 weeks][6]*

KEY

- PEG-IFN - peginterferon alfa-2a
- RBV – ribavirin

[1] Medicines for the treatment of hepatitis C are listed for prescribing by authorised nurse practitioners under the General Schedule only. Medicines for the treatment of hepatitis C are not listed for prescribing by authorised nurse practitioners under the S100 Highly Specialised Drugs Program.

[2][LEDIPASVIR + SOFOSBUVIR] for treatment-naïve, non-cirrhotic patients:

- consider treatment for 8 weeks where pre-treatment HCV RNA is less than 6 million IU/mL;
- otherwise treatment for 12 weeks where pre-treatment HCV RNA is 6 million IU/mL or greater.

[3][PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR] for treatment-naïve and treatment experienced, non-cirrhotic patients, treatment for 12 weeks in patients with genotype 1b HCV.

[4] [PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR (&) RBV] for treatment-naïve and treatment experienced, non-cirrhotic patients, treatment for 12 weeks in patients with genotype 1a HCV.

[5] [GRAZOPREVIR + ELBASVIR and RBV] for treatment-experienced, non-cirrhotic and cirrhotic patients, treatment for 16 weeks in patients with genotype 1a or 4 HCV who have experienced on-treatment virologic failure to prior treatment.

[6] [GLECAPREVIR + PIBRENTASVIR] for treatment experienced patients with genotype 3 HCV and patients who have failed an NS5A inhibitor, treatment is for 16 weeks.

[7][SOFOSBUVIR + VELPATASVIR] for patients with decompensated cirrhosis:

- Use in combination with ribavirin.

[8] [PARITAPREVIR + RITONAVIR + OMBITASVIR (&) DASABUVIR (&) RBV] for treatment-experienced, cirrhotic patients:

- consider treatment for 12 weeks in patients with genotype 1a HCV (except prior null responders to PEG-IFN and RBV) and genotype 1b HCV; or
- consider treatment for 24 weeks in patients with genotype 1a HCV who have had a previous null response to PEG-IFN and RBV.

[9] Consider a 24 week regimen of [DACLATASVIR and SOFOSBUVIR and RBV] for cirrhotic patients where clinically appropriate.

[10][SOFOSBUVIR + VELPATASVIR] for patients with genotype 3 infection with compensated cirrhosis:

- Consider addition of ribavirin.

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 PBAC recommendation to extend the PBS listing of Maviret to include patients with HCV, previously treated with an NS5A containing regimen.