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Appendix

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Appendix to: Thompson AJV; Expert panel representing the Gastroenterological Society of Australia (Australian Liver Association), Australasian Society for Infectious Diseases, Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine, Australasian Hepatology Association, Hepatitis Australia and Royal Australian College of General Practitioners. Australian recommendations for the management of hepatitis C virus infection: a consensus statement. *Med J Aust* 2016; 204. doi: 10.5694/mja16.00106.

Appendix 1. Treatment protocols for people with compensated liver disease and hepatitis C virus (HCV) genotype (Gt) 1 infection, including people with HCV–HIV coinfection

		Treatment duration				
		No cirrhosis		Cirrhosis		
Regimen	HCV Gt	Treatment-naive	Treatment-experienced*	Treatment-naive	Treatment-experienced*	Efficacy (SVR)
Sofosbuvir 400 mg, orally, daily + Ledipasvir 90 mg, orally, daily	1a/b	8 weeks OR 12 weeks‡	12 weeks§	12 weeks	24 weeks§	≥ 95%
Sofosbuvir 400 mg, orally, daily + Daclatasvir 60 mg, orally, daily† ± Ribavirin 1000/1200 mg, orally, daily (weight-based)††	1a/b	12 weeks	12 weeks OR 24 weeks¶	12 weeks + ribavirin OR 24 weeks (no ribavirin)	12 weeks + ribavirin OR 24 weeks (no ribavirin)¶	≥ 95%
Paritaprevir–ritonavir (150 mg/100 mg), orally, daily + Ombitasvir 25 mg, orally, daily + Dasabuvir 250 mg, orally, twice daily ± Ribavirin 1000/1200 mg, orally, daily (weight-based)††	1a	12 weeks + ribavirin	12 weeks + ribavirin	12 weeks + ribavirin	12 or 24 weeks + ribavirin**	≥ 95%
	1b	12 weeks	12 weeks	12 weeks	12 weeks	

HIV = human immunodeficiency virus. SVR = sustained virological response at least 12 weeks after treatment. PBS = Pharmaceutical Benefits Scheme. pegIFN = peginterferon-alfa. PrOD = paritaprevir (ritonavir-boosted) + ombitasvir + dasabuvir.

* Treatment experience may include a number of different treatment regimens; PBS eligibility and recommended duration for specific regimens varies according to the treatment history.

† Daclatasvir dose modification is required when used in combination with specific antiretroviral therapies for HIV (see consensus statement).

‡ 8 weeks may be considered if HCV RNA level is $< 6 \times 10^6$ IU/mL in people with no cirrhosis who are treatment-naive. 8-week treatment duration is not recommended for people with HCV–HIV coinfection.

§ Sofosbuvir + ledipasvir can be used to treat people in whom either pegIFN + ribavirin dual therapy or protease inhibitor + pegIFN + ribavirin triple therapy has failed.

¶ Sofosbuvir + daclatasvir (no ribavirin) for 12 weeks is recommended for people with no cirrhosis in whom pegIFN + ribavirin or sofosbuvir + ribavirin has previously failed; 24 weeks (no ribavirin) is recommended for people with cirrhosis in whom pegIFN + ribavirin has previously failed; 24 weeks (no ribavirin) is recommended for all people in whom a protease inhibitor + pegIFN + ribavirin has failed.

** The recommended treatment duration for PrOD plus ribavirin in people with Gt 1a HCV and cirrhosis who have had a previous null response to pegIFN and ribavirin therapy is 24 weeks. PrOD therapy is not recommended for people who did not respond to previous therapy that included an HCV protease inhibitor or an NS5A inhibitor.

†† Ribavirin dosing is weight-based; recommended dose is 1000 mg for people weighing < 75 kg and 1200 mg for people weighing ≥ 75 kg.

Notes: For Gt 1 HCV patients in whom treatment with a protease inhibitor + pegIFN + ribavirin has failed, the preferred treatment is sofosbuvir + ledipasvir or sofosbuvir + daclatasvir. Sofosbuvir is not recommended for patients with an estimated glomerular filtration rate < 30 mL/min/1.73 m^2. Dose reduction or dose interruption of direct-acting antiviral therapy is not recommended. Dose reduction of ribavirin for the management of symptomatic anaemia according to the product information is appropriate and will not reduce the likelihood of SVR. PrOD should only be used to treat people who are treatment-naive or people who have previously not responded to pegIFN + ribavirin. At the time of writing, the combination of PrOD ± ribavirin was approved by the Therapeutic Goods Administration but not yet available for prescription under the PBS.

Appendix 2. Treatment protocols for people with compensated liver disease and hepatitis C virus (HCV) genotype (Gt) 2 or 3 infection, including people with HCV–HIV coinfection

		Treatment duration				
		No cirrhosis		Cirrhosis		
Regimen	HCV Gt	Treatment-naive	Treatment-experienced*	Treatment-naive	Treatment-experienced*	Efficacy (SVR)
Sofosbuvir 400 mg, orally, daily + Ribavirin 1000/1200 mg, orally, daily (weight-based)**	2	12 weeks	12 weeks§	12 weeks	12 weeks§	> 90%
Sofosbuvir 400 mg, orally, daily + Daclatasvir, 60 mg, orally, daily†	3	12 weeks	12 weeks¶	24 weeks	24 weeks¶	> 85%
Sofosbuvir 400 mg, orally, daily + Ribavirin 1000/1200 mg, orally, daily (weight-based)**	3	24 weeks	24 weeks§	24 weeks	24 weeks§	58%–95%‡
Sofosbuvir 400 mg, orally, daily + PegIFN, subcutaneously, weekly + Ribavirin 1000/1200 mg, orally, daily (weight-based)**	3	12 weeks	12 weeks††	12 weeks	12 weeks††	> 85%

SVR = sustained virological response at least 12 weeks after treatment. PBS = Pharmaceutical Benefits Scheme. pegIFN = peginterferon-alfa.

* Treatment experience may include a number of different treatment regimens; PBS eligibility and recommended duration for specific regimens varies according to the treatment history.

† Daclatasvir dose modification is required when used in combination with specific antiretroviral therapies for human immunodeficiency virus (HIV; see consensus statement).

‡ SVR rates vary from 90%–95% for treatment-naive individuals with no cirrhosis to 58%–76% for treatment-experienced individuals with cirrhosis.

§ Sofosbuvir + ribavirin can be used to treat people with Gt 2 or Gt 3 HCV in whom pegIFN + ribavirin dual therapy has failed.

¶ Sofosbuvir + daclatasvir (no ribavirin) for 12 weeks is recommended for people with no cirrhosis in whom pegIFN + ribavirin or sofosbuvir + ribavirin has previously failed; 24 weeks (no ribavirin) is recommended for people with cirrhosis in whom pegIFN + ribavirin or sofosbuvir + ribavirin has previously failed.

†† Sofosbuvir + pegIFN + ribavirin can be used to treat people in whom pegIFN + ribavirin only has previously failed.

** Ribavirin dosing is weight-based; recommended dose is 1000 mg for people weighing < 75 kg and 1200 mg for people weighing ≥ 75 kg.

Notes: Dose reduction or dose interruption of direct-acting antiviral therapy is not recommended. Dose reduction of ribavirin for the management of symptomatic anaemia according to the product information is appropriate and will not reduce the likelihood of SVR.

Appendix 3. Treatment protocols for people with compensated liver disease and hepatitis C virus (HCV) genotype (Gt) 4, 5 or 6 infection, including people with HCV–HIV coinfection

		Treatment duration				
		No cirrhosis		Cirrhosis		
Regimen	HCV Gt	Treatment-naive	Treatment-experienced*	Treatment-naive	Treatment-experienced*	Efficacy (SVR)
Sofosbuvir 400 mg, orally, daily + Peginterferon-alfa, subcutaneously, weekly + Ribavirin 1000/1200 mg, orally, daily (weight-based)‡	4, 5, 6	12 weeks	12 weeks	12 weeks	12 weeks	> 90%†

HIV = human immunodeficiency virus. SVR = sustained virological response at least 12 weeks after treatment.

* Treatment-experienced refers to prior peginterferon-alfa + ribavirin dual therapy.

† Of 35 treatment-naive patients with Gt 4, 5 or 6 HCV enrolled in the NEUTRINO study, 34 (97%) achieved SVR.[17] Treatment-experienced patients were not enrolled in the NEUTRINO study.

‡ Ribavirin dosing is weight-based; recommended dose is 1000 mg for people weighing < 75 kg and 1200 mg for people weighing ≥ 75 kg.

Notes: Dose reduction or dose interruption of direct-acting antiviral therapy is not recommended. Dose reduction of ribavirin for the management of symptomatic anaemia according to the product information is appropriate and will not reduce the likelihood of SVR.

Appendix 4. Monitoring of patients receiving antiviral therapy for hepatitis C virus (HCV) infection: (A) on-treatment and post-treatment monitoring for virological response; and (B) monitoring after SVR

A. On-treatment and post-treatment monitoring for virological response

Routine monitoring for a 12-week treatment regimen:

Week 0	• FBE, LFTs, INR, HCV RNA level (quantitative), renal function tests including eGFR and creatinine
Week 4	• FBE, LFTs
Week 12 ± 24 (EOT)	• FBE, LFTs, HCV PCR (qualitative)
	• At each on-treatment visit, assess for: ▸ medication adherence ▸ treatment adverse effects ▸ drug–drug interactions
Week 12 after EOT (SVR)	• FBE, LFTs, HCV PCR (qualitative)

- Routine on-treatment HCV RNA testing is not mandated but may be considered where there is a clinical concern about non-adherence to treatment, especially in people with cirrhosis.
- The need for increased frequency of review should be individualised.
- Patients taking ribavirin may require FBE at Week 2 and Week 4 and then every 4 weeks.
- Patients with cirrhosis require monitoring every 4 weeks, including FBE, LFTs and assessment for hepatic decompensation. Measurement of quantitative HCV RNA level is recommended at Weeks 4, 12 ± 24 on-treatment in patients with cirrhosis.
- Patients with decompensated liver disease require close monitoring, with review every 2–4 weeks.

B. Monitoring after SVR

SVR, no cirrhosis and normal LFT results (males, ALT < 30 U/L; females, ALT < 19 U/L):

- Patients who are cured do not require clinical follow-up for HCV

SVR and abnormal LFT results (males, ALT ≥ 30 U/L; females, ALT ≥ 19 U/L):

- Patients with persistently abnormal LFT results require evaluation for other liver diseases and should be referred for gastroenterology review. Investigations to consider include: fasting glucose level, fasting lipid levels, iron studies, ANA, ASMA, anti-LKM antibodies, total IgG and IgM, AMA, coeliac serology, copper level, caeruloplasmin level and α-1-antitrypsin level

SVR, cirrhosis:

- Patients with cirrhosis require long-term monitoring and should be enrolled in screening programs for:
  - hepatocellular carcinoma — liver ultrasound ± serum α-fetoprotein level
  - oesophageal varices — gastroscopy
  - osteoporosis — dual emission x-ray absorptiometry

EOT = end of treatment. SVR = sustained virological response at least 12 weeks after treatment (cure). FBE = full blood examination. LFT = liver function test. INR = international normalised ratio. eGFR = estimated glomerular filtration rate. PCR = polymerase chain reaction. ALT = alanine aminotransferase. ANA = anti-nuclear antibodies. ASMA = anti-smooth muscle antibodies. LKM = liver–kidney microsome. AMA = anti-mitochondrial antibody.