Clinical guidance for treating hepatitis C virus infection: a summary

Six key questions before commencing treatment for hepatitis C virus (HCV) infection

- Is cirrhosis present?
- What is the HCV genotype?
- Is the patient treatment-naive?
- Is HBV–HCV or HIV–HCV coinfection present?
- Are there potential drug–drug interactions?
- What is the renal function (eGFR)?

Checklist for pre-treatment assessment for people with hepatitis C virus (HCV) infection

	HCV virology: • Anti-HCV (serology) • HCV PCR • HCV genotype, quantitative HCV RNA level*	 • Indicates HCV exposure • Confirms HCV infection • May influence choice and duration of treatment regimen
	HCV treatment history — previous regimen and response	Determines treatment regimen and duration
	Potential for non-adherence?	Consider medical and social issues that may be barriers to medication adherence
	Alcohol intake history	Cofactor for cirrhosis
	Check for drug–drug interactions	**www.hep-druginteractions.org** Includes prescribed, over-the-counter, herbal, illicit drugs
	Pregnancy discussion†	
	Weight and body mass index	Non-alcoholic fatty liver disease is a cofactor for cirrhosis
	Signs of chronic liver disease	
	FBE	• Baseline haemoglobin level • Low platelets — suspect portal hypertension
	LFTs and INR	Low albumin, raised bilirubin, raised INR suggest advanced cirrhosis
	U&Es and eGFR	• Sofosbuvir is not recommended if eGFR < 30 mL/min/1.73 m^2 • Ribavirin is renally cleared and needs dose reduction if eGFR < 50 mL/min/1.73 m^2
	HBV (HBsAg, anti-HBc, anti-HBs), HIV, HAV serology	Specialist referral is recommended for people with HBV or HIV coinfection If seronegative, vaccinate against HAV, HBV
	Cirrhosis assessment • e.g. FibroScan • e.g. APRI	Thresholds consistent with no cirrhosis: • Liver stiffness < 12.5 kPa • APRI < 1.0 Specialist referral is recommended for people with cirrhosis
	Electrocardiogram if ribavirin therapy planned and patient is aged > 50 years OR has cardiac risk factors	Screen for ischaemic heart disease

FBE = full blood examination. LFT = liver function test. INR = international normalised ratio. U&E = urea and electrolyte. eGFR = estimated glomerular filtration rate. HBV = hepatitis B virus. HAV = hepatitis A virus. HBsAg = hepatitis B surface antigen. anti-HBc = hepatitis B core antibody. anti-HBs = hepatitis B surface antibody. APRI = aspartate aminotransferase to platelet ratio index. MELD = Model for End-Stage Liver Disease. HCC = hepatocellular carcinoma. * HCV genotype is required by the PBS criteria; it is important before prescribing elbasvir plus grazoprevir or sofosbuvir plus ledipasvir. HCV RNA level is important for determining eligibility for 8-week treatment duration with sofosbuvir plus ledipasvir. † As there are no safety data for the use of any direct-acting antiviral regimen during pregnancy, treatment of pregnant women is not recommended. Ribavirin (Category X) and peginterferon-alfa are contraindicated during pregnancy.

Support for people living with hepatitis C

People living with hepatitis C can receive information, support and referral from community services, including:

- Hepatitis Australia: http://www.hepatitisaustralia.com
- Hepatitis Information Line: 1800 437 222
- Australian Injecting & Illicit Drug Users League: http://www.aivl.org.au

On-treatment and post-treatment monitoring for virological response

Routine monitoring for a 12-week treatment regimen:

Week 0	• Pre-treatment blood tests, including LFTs, HCV PCR
Week 12 post-treatment (SVR)	• LFTs, HCV PCR (qualitative)

- More intensive monitoring may be required in certain populations (see *Australian recommendations for the management of hepatitis C virus infection: a consensus statement* (September 2018), http://www.gesa.org.au).
- People treated with elbasvir plus grazoprevir should have LFTs at Week 8 to screen for hepatotoxicity.

SVR = sustained virological response at least 12 weeks after treatment (cure). LFT = liver function test. INR = international normalised ratio. HCV = hepatitis C virus. PCR = polymerase chain reaction.

Ongoing monitoring of people after successful hepatitis C treatment outcome (SVR)

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

- People who are cured do not require clinical follow-up for hepatitis C

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 and cirrhosis:

- Patients with cirrhosis require long-term monitoring and should be enrolled in screening programs for:
  - hepatocellular carcinoma
  - oesophageal varices
  - osteoporosis

SVR = sustained virological response at least 12 weeks after treatment (cure). LFT = liver function test. ALT = alanine aminotransferase. ANA = anti-nuclear antibodies. ASMA = anti-smooth muscle antibodies. LKM = liver–kidney microsome. AMA = anti-mitochondrial antibody.

People who do not respond to hepatitis C treatment

- Specialist referral recommended

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Recommended treatment protocols for treatment-naive people with hepatitis C virus (HCV) infection and compensated liver disease, including people with HCV–HIV coinfection

		Treatment duration	
Regimen	HCV genotype	No cirrhosis	Cirrhosis
Sofosbuvir 400 mg, orally, daily + Velpatasvir 100 mg, orally, daily	1, 2, 3, 4, 5, 6	12 weeks	12 weeks*
Glecaprevir 300 mg, orally, daily + Pibrentasvir 120 mg, orally, daily	1, 2, 3, 4, 5, 6	8 weeks	12 weeks
Elbasvir, 50 mg, orally, daily + Grazoprevir, 100 mg, orally, daily	1, 4	12 weeks	12 weeks
Sofosbuvir 400 mg, orally, daily + Ledipasvir 90 mg, orally, daily	1	8 or 12 weeks†	12 weeks

HIV = human immunodeficiency virus.

* Addition of ribavirin may be considered for patients with genotype 3 HCV and compensated cirrhosis. Ribavirin dosing is weight-based; recommended dose is 1000 mg for people weighing < 75 kg and 1200 mg for people weighing ≥ 75 kg.

† 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.

Notes:

- 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.
- The recommended treatment regimens differ in the setting of decompensated liver disease (Child–Pugh score ≥ B7) (see *Australian recommendations for the management of hepatitis C virus infection: a consensus statement* (September 2018), http://www.gesa.org.au).

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