Clinical guidance for treating hepatitis C virus infection: a summary

Four key questions before commencing pan-genotypic treatment for hepatitis C virus (HCV) infection

- Is cirrhosis present?
- Is the patient treatment-naive?
- Is HBV–HCV or HIV–HCV coinfection present?
- Are there potential drug–drug interactions?

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

☐	HCV virology: • Anti-HCV (serology) • HCV PCR • HCV genotype (where possible)	 • Indicates HCV exposure • Confirms current 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	• Patients with comorbidities or with advanced liver disease are at risk of chronic kidney disease • Rarely, chronic HCV infection is associated with kidney disease
☐	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

anti-HBc = hepatitis B core antibody; anti-HBs = hepatitis B surface antibody; APRI = aspartate aminotransferase to platelet ratio index; eGFR = estimated glomerular filtration rate; FBE = full blood examination; HAV = hepatitis A virus; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; INR = international normalised ratio; LFT = liver function test; MELD = Model for End-Stage Liver Disease; U&E = urea and electrolyte.

* As there are no safety data for the use of any direct-acting antiviral regimen during pregnancy, treatment of pregnant women is not recommended.

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 an 8–12-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* (May 2020), http://www.gesa.org.au).

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

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 and risk of reinfection:

- Patients with ongoing risk of HCV infection should have at least annual HCV RNA testing
- Anti-HCV antibodies will remain positive in all people with prior exposure and this does not require repeated testing

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

People who do not respond to hepatitis C treatment

- Specialist referral recommended

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Recommended pan-genotypic 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	Pill burden	No cirrhosis	Cirrhosis
Sofosbuvir 400 mg, orally, daily + Velpatasvir 100 mg, orally, daily	1, 2, 3, 4, 5, 6	1 pill daily	12 weeks	12 weeks†
Glecaprevir 300 mg, orally, daily + Pibrentasvir 120 mg, orally, daily	1, 2, 3, 4, 5, 6	Once daily (3 pills)	8 weeks	12 weeks

HIV = human immunodeficiency virus. * Dose reduction or dose interruption of direct-acting antiviral therapy is not recommended.

† 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.