Clinical guidance for treating hepatitis C virus infection: a summary

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

	HCV virology: • Anti-HCV (serology) • HCV RNA level (quantitative) • HCV genotype	 • Indicates HCV exposure • Confirms HCV infection • Determines 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
	Weight and body mass index	Non-alcoholic fatty liver disease (NAFLD) — cofactor for cirrhosis
	Pregnancy discussion*	
	Check for drug–drug interactions	**www.hep-druginteractions.org** Includes prescribed, over-the-counter, complementary/herbal, illicit drugs
	Signs of chronic liver disease	
	FBE	• Baseline haemoglobin level • Low platelets are a marker of portal hypertension
	LFTs and INR	Low albumin, raised bilirubin, raised INR identify liver synthetic dysfunction and 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
	Fasting glucose and lipids	Diabetes and hyperlipidaemia are associated with NAFLD
	HBV (HBsAg, anti-HBc, anti-HBs), HIV, HAV serology	If seronegative, vaccinate against HAV, HBV
	Cirrhosis assessment • FibroScan • APRI	Determines treatment regimen and duration Thresholds consistent with no cirrhosis: • Liver stiffness < 12.5 kPa • APRI < 1.0
	If cirrhosis present: • Specialist referral recommended • MELD and Child–Pugh scores • Liver ultrasound • Gastroscopy • Bone densitometry scan	 • Prognostic scores indicating liver decompensation • Screen for HCC, portal hypertension • Screen for oesophageal varices • Screen for osteoporosis
	Electrocardiogram if ribavirin therapy planned and patient is aged > 50 years OR has cardiac risk factors	Screen for ischaemic heart disease

* 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. Both women and men should be counselled about the risk of teratogenicity and the importance of avoiding pregnancy during treatment, and for 6 months after ribavirin treatment. Women treated with paritaprevir–ritonavir, ombitasvir and dasabuvir should avoid ethinyl estradiol-containing contraceptives.

HCV = hepatitis C virus. 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.

On-treatment and post-treatment monitoring for virological response

Routine monitoring for a 12-week treatment regimen:	
Week 0	• FBE, U&Es, LFTs, INR, HCV RNA level (quantitative)
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. People taking ribavirin may require FBE at Week 2 and Week 4 and then every 4 weeks. People 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. People with cirrhosis who are treated with the combination of paritaprevir–ritonavir, ombitasvir, dasabuvir ± ribavirin should have LFTs checked at Week 2 as well as Week 4. People with decompensated liver disease require close monitoring, with review every 2–4 weeks.

EOT = end of treatment. SVR = sustained virological response at least 12 weeks after treatment (cure). FBE = full blood examination. U&E = urea and electrolyte. 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):

- People 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, caeruloplasmin and α-1-antitrypsin levels.

SVR, cirrhosis:

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

Regimen	HCV genotype	No cirrhosis		Cirrhosis	
		Treatment-naive	Treatment-experienced*	Treatment-naive	Treatment-experienced*
Sofosbuvir 400 mg, orally, daily + Ledipasvir 90 mg, orally, daily	1a/b	8 or 12 weeks†	12 weeks	12 weeks	24 weeks
Sofosbuvir 400 mg, orally, daily + Daclatasvir 60 mg, orally, daily‡ ± Ribavirin 1000/1200 mg, orally, daily§	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)
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§	1a	12 weeks + ribavirin	12 weeks + ribavirin	12 weeks + ribavirin	12 or 24 weeks + ribavirin**
	1b	12 weeks	12 weeks	12 weeks	12 weeks
Sofosbuvir 400 mg, orally, daily + Ribavirin 1000/1200 mg, orally, daily§	2	12 weeks	12 weeks	12 weeks	12 weeks
Sofosbuvir 400 mg, orally, daily + Daclatasvir, 60 mg, orally, daily‡	3	12 weeks	12 weeks	24 weeks	24 weeks
Sofosbuvir 400 mg daily + Ribavirin 1000/1200 mg daily§	3	24 weeks	24 weeks	24 weeks	24 weeks
Sofosbuvir 400 mg, orally, daily + Peginterferon-alfa, subcutaneously, weekly + Ribavirin 1000/1200 mg, orally, daily§	3, 4, 5, 6	12 weeks	12 weeks	12 weeks	12 weeks

* Treatment experience generally refers to peginterferon-alfa plus ribavirin ± first-generation protease inhibitors (see full consensus statement). † 8 weeks may be considered if HCV RNA < 6×10^6 IU/mL in people with no cirrhosis who are treatment-naive. ‡ Daclatasvir dose modification is required when used in combination with specific antiretroviral therapies for HIV (see full consensus statement). § Ribavirin dosing is weight-based; recommended dose is 1000 mg for people weighing < 75 kg and 1200 mg for people weighing ≥ 75 kg. ¶ Recommended treatment duration for sofosbuvir plus daclatasvir (no ribavirin) for people who have failed treatment with a protease inhibitor + peginterferon-alfa + ribavirin is 24 weeks, including people with cirrhosis and people with no cirrhosis; recommended treatment duration for people with no cirrhosis who have previously failed peginterferon-alfa + ribavirin is 12 weeks. ** Recommended treatment duration for paritaprevir–ritonavir, ombitasvir, dasabuvir (PrOD) plus ribavirin in people with genotype 1a HCV and cirrhosis who have had a previous null response to peginterferon-alfa 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.

Notes: Sofosbuvir is not recommended for patients with an estimated glomerular filtration rate < 30 mL/min/1.73 m². 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 Pharmaceutical Benefits Scheme; this treatment regimen should be used with caution in people with cirrhosis and is contraindicated in people with decompensated liver disease. 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 (sustained virological response at least 12 weeks after treatment [cure]).
The recommended treatment regimens differ in the setting of decompensated liver disease (Child–Pugh score ≥ B7) (see full consensus statement).

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