Clinical guidance for treating hepatitis C virus infection: a summary

For more information: www.gesa.org.au or gesa@gesa.org.au

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

- What is the HCV genotype?
- Is cirrhosis present?
- 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 HCV infection

HCV virology:
- Anti-HCV (serology)
- HCV RNA level (quantitative)
- HCV genotype

HCV treatment history — previous regimen and response

Potential for non-adherence?

Check for drug–drug interactions

www.hep-druginteractions.org

Includes prescribed, over-the-counter, herbal, illicit drugs

Pregnancy discussion*

Weight and body mass index

Signs of chronic liver disease

FBE

LFTs and INR

U&Es and eGFR

HBV (HBsAg, anti-HBc, anti-HBs), HIV, HAV serology

Cirrhosis assessment

- FibroScan
- APRI

Electrocardiogram if ribavirin therapy planned and patient is aged > 50 years OR has cardiac risk factors

On-treatment and post-treatment monitoring for virological response

Routine monitoring for a 12-week treatment regimen:

Week 0
- FBE, U&Es, LFTs, HCV RNA level (quantitative)

Week 4*
- LFTs
- At each on-treatment visit, assess for:
  - medication adherence
  - treatment adverse effects
  - drug–drug interactions

Week 12 (EOT)
- LFTs
- HCV PCR (qualitative)

Week 12 after EOT (SVR)
- LFTs, HCV PCR (qualitative)

EOT = end of treatment. SVR = sustained virological response at least 12 weeks after treatment (cure).

Week 4 LFTs may be done as an alternative to Week 4 LFTs.

People who do not respond to hepatitis C treatment

• Specialist referral recommended

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

People who do not respond to hepatitis C treatment

- Specialist referral recommended

FBE = full blood examination. LFT = liver function test. INR = international normalised ratio. U&E = urea and electrolyte. eGFR = estimated glomerular filtration rate. HCV = hepatitis C virus. HAV = hepatitis A virus. HBV = hepatitis B 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. * 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.

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<table>
<thead>
<tr>
<th>Regimen</th>
<th>HCV genotype</th>
<th>No cirrhosis</th>
<th>Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Treatment-naive</td>
<td>Interferon-experienced</td>
</tr>
<tr>
<td>Sofosbuvir 400 mg, orally, daily + Velpatasvir 100 mg, orally, daily</td>
<td>1, 2, 3, 4, 5, 6*</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Sofosbuvir 400 mg, orally, daily + Ledipasvir 90 mg, orally, daily</td>
<td>1a/b</td>
<td>8 or 12 weeks†</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Elbasvir 50 mg, orally, daily + Grazoprevir 100 mg, orally, daily ± Ribavirin 1000/1200 mg, orally, daily</td>
<td>1a</td>
<td>12 weeks</td>
<td>12 weeks (relapser) or 16 weeks + ribavirin (OTVF)</td>
</tr>
<tr>
<td>Sofosbuvir 400 mg, orally, daily + Daclatasvir 60 mg, orally, daily ± Ribavirin 1000/1200 mg, orally, daily*</td>
<td>1a/b</td>
<td>12 weeks</td>
<td>12 or 24 weeks§</td>
</tr>
<tr>
<td>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*</td>
<td>1b</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Sofosbuvir 400 mg, orally, daily + Daclatasvir 60 mg, orally, daily ± Ribavirin 1000/1200 mg, orally, daily*</td>
<td>3</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Elbasvir 50 mg, orally, daily + Grazoprevir 100 mg, orally, daily ± Ribavirin 1000/1200 mg, orally, daily*</td>
<td>4</td>
<td>12 weeks</td>
<td>12 weeks (relapser) or 16 weeks + ribavirin (OTVF)</td>
</tr>
</tbody>
</table>

SVR = sustained virological response at least 12 weeks after treatment (cure). Relapser = patient who failed to achieve SVR despite achieving an on-treatment response. OTVF = on-treatment virological failure (patient who has had a null response, partial response, virological breakthrough or rebound, or intolerance to prior treatment).

- Patients with mixed HCV genotype infection or in whom HCV genotype cannot be determined should be treated with sofosbuvir plus velpatasvir for 12 weeks.
- Addition of ribavirin may be considered for patients with genotype 3 HCV and compensated cirrhosis.
- 8 weeks may be considered if HCV RNA < 6 x 10^6 IU/mL in people with no cirrhosis who are treatment-naive.
- Ribavirin dosing is weight-based; recommended dose is 1000 mg for people weighing < 75 kg and 1000 mg for people weighing ≥ 75 kg.
- Daclatasvir dose modification is required when used in combination with specific antiretroviral therapies for HIV (see full consensus statement).
- 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 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 full consensus statement).