Guidelines for management of chronic HCV infection

Headline Recommendations

1. We recommend that NHSE considers commissioning pan-genotypic regimens for use in the community for patients who are treatment naïve and do not have cirrhosis to avoid the need for genotyping and facilitate rapid access to care.

2. We recommend that ribavirin be avoided whenever possible.

3. We recommend that 8 week regimens without ribavirin are first choice for treatment naïve non-cirrhotic patients treated in community or prison settings regardless of genotype.

4. We reiterate that transplantation is not contra-indicated in patients with HCV even in the presence of ‘difficult’ drug resistant mutations.

5 Drug-drug interactions should continue to be assessed and therapy should take account of potential interactions.

Genotype Specific Recommendations

Non-cirrhotic

G1a
Sofosbuvir/ledipasvir 8 weeks (treatment naïve) or 12 weeks (treatment experienced)
Grazoprevir/elbasvir 12 weeks OR 16 weeks + ribavirin for patients with viral load >800,000 and resistance associated substitutions (16 weeks + ribavirin is NOT a preferred regimen)
Paritaprevir/ritonavir/ombitasvir+dasabuvir+ribavirin 12 weeks – should be discarded when Glecaprevir/pibrentasvir is available.
Sofosbuvir/velpatasvir 12 weeks
Sofosbuvir/velpatasvir/voxilaprevir - 8 weeks
Glecaprevir/pibrentasvir - 8 weeks
**G1b**
Sofosbuvir/ledipasvir 8 weeks (treatment naïve) or 12 weeks (treatment experienced)
Grazoprevir/elbasvir 12 weeks
Paritaprevir/ritonavir/ombitasvir+dasabuvir 12 weeks – should be discarded when Glecaprevir/pibrentasvir is available.
Sofosbuvir/velpatasvir 12 weeks
Sofosbuvir/velpatasvir/voxilaprevir 8 weeks
Glecaprevir/pibrentasvir 8 weeks

**Compensated cirrhosis**

**G1a**
Sofosbuvir/ledipasvir 12 weeks
Grazoprevir/elbasvir 12 weeks OR 16 weeks + ribavirin for patients with viral load >800,000 and resistance associated substitutions (16 weeks + ribavirin is NOT a preferred regimen)
Paritaprevir/ritonavir/ombitasvir+dasabuvir+ribavirin 12-24 weeks - should be discarded when Glecaprevir/pibrentasvir is available.
Sofosbuvir/velpatasvir 12 weeks
Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Glecaprevir/pibrentasvir 12 weeks

**G1b**
Sofosbuvir/ledipasvir 12 weeks
Grazoprevir/elbasvir 12 weeks
Paritaprevir/ritonavir/ombitasvir+dasabuvir 12 weeks - should be discarded when Glecaprevir/pibrentasvir is available.
Sofosbuvir/velpatasvir 12 weeks
Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Glecaprevir/pibrentasvir 12 weeks

** Decompensated cirrhosis G1a &1b**
Sofosbuvir/ledipasvir +/- ribavirin 12 weeks
Sofosbuvir/velpatasvir + ribavirin 12 weeks

**Re-treatment for DAA failures**
Requires pre-treatment virological sequencing to identify resistance associated variants whose presence/absence should be used to guide treatment decisions.

Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Glecaprevir/pibrentasvir 12 weeks (no prior NS5A) or 16 weeks (prior NS5A)

Decompensated cirrhosis – retreatment requires Sof/vel +/- riba 24 weeks
**G2**

**Non cirrhotic**
Strongly recommend that IFN is removed and ribavirin free regimens are preferred.
Sof/Vel 12 weeks
Sof/Vel/Vox 8 weeks
Glecaprevir/pibrentasvir 8 weeks

**Cirrhosis**
Sof/Vel 12 weeks
Sof/vel/vox 12 weeks
Glecaprevir/pibrentasvir 12 weeks

** Decompensated cirrhosis**
Sof/vel +/- riba 12 weeks

**Re-treatment of DAA failures**
Requires pre-treatment virological sequencing to identify resistance associated variants whose presence/absence should be used to guide treatment decisions.

Sofosbuvir/velpatasvir/voxilaprevir **12 weeks**
Glecaprevir/pibrentasvir 16 weeks

**G3**

**Non cirrhotic**
Sof/Vel 12 weeks
Sof/Vel/Vox 8 weeks
Glecaprevir/pibrentasvir 8 weeks

**Cirrhotic**
Sof/Vel 12 weeks
Sof/Vel/Vox 12 weeks
Glecaprevir/pibrentasvir 16 weeks

** Decompensated cirrhosis**
12 weeks sofosbuvir/velpatasvir +ribavirin.
Consideration should be given to the use of sof/vel for 24 weeks in patients deemed unlikely to respond or intolerant of ribavirin.

**Re-treatment for DAA failures**
Requires pre-treatment virological sequencing to identify resistance associated variants whose presence/absence should be used to guide treatment decisions.

Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Decompensated cirrhosis – retreatment requires Sof/vel +/- riba 24 weeks

G4

**Non Cirrhotic**
Given the paucity of data and the availability of better-validated regimens we recommend that the use of sofosbuvir/ledipasvir for patients with Genotype 4 HCV should be discontinued.

Grazoprevir/elbasvir 12
Paritaprevir/ritonavir/ombitasvir 12 weeks - should be discarded when Glecaprevir/pibrentasvir is available.
Sofosbuvir/velpatasvir/voxilaprevir 8 weeks
Sofosbuvir/velpatasvir 12 weeks
Glecaprevir/pibrentasvir 8 weeks

**Cirrhosis**
Grazoprevir/elbasvir 12 OR 16 weeks
Sofosbuvir/velpatasvir 12 weeks
Paritaprevir/ritonavir/ombitasvir 12 weeks - should be discarded when Glecaprevir/pibrentasvir is available.
Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Glecaprevir/pibrentasvir 12 weeks

** Decompensated cirrhosis**
12 weeks sofosbuvir/velpatasvir +ribavirin.

**Re-treatment for DAA failures**
Requires pre-treatment virological sequencing to identify resistance associated variants whose presence/absence should be used to guide treatment decisions.

Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Glecaprevir/pibrentasvir 16 weeks

G5/6
The small number of patients G5/6 infection in trials reported to date was noted.

**Non cirrhotic**
Sof/Vel 12 weeks
Glecaprevir/pibrentasvir 8-12 weeks
Sof/Vel/Vox 8 weeks

**Cirrhotic**
Sofosbuvir/velpatasvir 12 weeks
Glecaprevir/pibrentasvir 12 weeks
Sof/vel/vox 8 weeks

**Decompensated cirrhosis**
12 weeks sofosbuvir/velpatasvir +ribavirin.
Re-treatment for DAA failures
Requires pre-treatment virological sequencing to identify resistance associated variants whose presence/absence should be used to guide treatment decisions.

Sofosbuvir/velpatasvir/voxilaprevir 12 weeks
Glecaprevir/pibrentasvir 16 weeks (note that in patients with both NS5A and NS3 resistance associated variants this regimen is likely to be inadequate)

Special Patient Categories

Patients with renal impairment
We recommend treatment as above but recommend that sofosbuvir be avoided in patients with GFR <45 ml/min.

HIV-hepatitis C coinfection
We recommend that patients with HIV-hepatitis C coinfection are treated for chronic hepatitis C with the same DAA-based treatment regimens as patients with hepatitis C mono-infection, although consideration of drug-drug interactions between DAAs and antiretrovirals should be taken into account.

We recommend that where HIV therapy cannot be switched to avoid drug-drug interactions, an appropriate alternate DAA-based regimen is identified.

Acute hepatitis C infection
We note emerging data shows public health benefits with early DAA therapy for patients with acute HCV who are at high risk of transmission. We recognize that pegylated interferon and ribavirin (the only current treatment option) is unlikely to be acceptable to patients and we therefore recommend that DAA-based treatment is made available for the treatment of acute and early hepatitis C infection, replacing pegylated-interferon +/- ribavirin 24 to 48 weeks

Re-infection following successful DAA-based hepatitis C treatment
We recommend that DAA-based treatment is made available for the treatment of hepatitis C re-infection following successful DAA-based hepatitis C treatment.
Solid Organ Transplantation

HCV infection acquired from a donor organ can be readily treated with currently available drug regimens. We recommend that patients without HCV infection should be offered an opportunity to receive an organ infected with HCV and we recommend that such recipients are offered antiviral therapy as soon as practicable post transplantation; with usual practice being to initiate treatment within the first month.