Preface

These guidelines were generated following a consensus meeting held in Birmingham on the 30th of June 2017 of representatives from the above organisations as well as representatives from the operational delivery networks in England. They are intended to reflect best practice rather than what is currently commissioned for HCV treatment.

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+ribavirin 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

**G2 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.