Hepatitis C - Full Clinical Guideline

Reference no.: CG-T/2012/199

The majority of acute infections are asymptomatic and acute fulminant liver failure is extremely rare. 20-40% of patients will spontaneously clear the virus (remain anti-HCV antibody positive) within the first 6 months, while the remainder continue with a chronic hepatitis and are at risk of progressive liver fibrosis leading (usually over decades) to cirrhosis and HCC.

Diagnosis: Anti-HCV antibodies are the first line diagnostic test. If positive then HCV RNA should be determined to see if infection is ongoing.

Anti-HCV positive, HCV RNA negative patients should be retested for HCV RNA after 3/12 to confirm spontaneous clearance.

Initial clinic visit assessment:

- Elicit likely route of infection - ongoing risk?
- Alcohol consumption should be assessed and quantified
- Ensure accurate drug history - Directly- Acting Antiviral (DAA) treatment is associated with multiple drug-drug interactions
- Check HBsAg, HIV, HCV viral genotype - if not already done
- Assessment of liver disease severity with Fibroscan

Treatment:

- Is the patient willing and physically, psychologically and socially fit for treatment (active substance use is not an absolute contraindication to treatment, but there must be stability to their substance use, existing patient support and steps in place to avoid re-infection)

- Patients deemed suitable for treatment should be discussed at the RDH Viral hepatitis MDT (Wed am 08.30-09.30). Patients can be put on the MDT by emailing the viral hepatitis specialist nurses or if you have access to the Gastroenterology shared drive then the MDT list is found under (Hepatology – Viral hepatitis service – Viral MDT – HCV MDT Live).

- Patients recommended for DAA treatment will then be presented by the viral hepatitis nurse specialists via teleconference to the regional Operational Delivery Network (ODN) MDT, held at 13.00 every Thursday

- Treatment options are dictated by NHS England Specialised Commissioning Group and are updated quarterly. Stage of disease is a factor in determining the choice of treatment:

  F3 = Liver biopsy Ishak stage 4 or FibroScan median TE > 9.5 kPa but ≤ 11.5kPa
  Cirrhosis = Liver biopsy Ishak stage 5 or 6, Fibroscan median TE > 11.5kPa,
  AST/ ALT > 1.0 and APRI score > 2, radiological evidence of cirrhosis or
  evidence of portal hypertension without alternative cause.

- The choice of treatment should also take into account absolute and relative contraindications and potential drug-drug interactions. These are frequent with DAA treatment and review of all co-administered drugs using www.hep-druginteractions.org is required.

- Indications for HCV treatment in HIV and HBV co-infected patients is identical to those with monoinfection. Drug interactions are a key consideration in treating patients with HIV-HCV co-infection where co-administration with some HIV drugs is contraindicated

- If DAA treatment is recommended then a blueteq code needs to be generated through the NHS High cost drug database (https://www.blueteq-secure.co.uk/Trust/default.aspx). This code needs to be entered on the EPMA prescription before the drugs will be dispensed.

Directly Active Antiviral (DAA) therapy

There are 3 classes of DAA treatment. Drugs from different classes are used in combination to achieve an SVR. See Table 3 for details of available treatment regimens

NS5B polymerase inhibitor (end with BUVIR)	Nucleotide - Sofobuvir Non-Nucleotide - Dasabuvir
NS5A inhibitor (end with ASVIR)	Ledipasvir Velpatasvir Elbasvir Ombitasvir Daclatasvir Pibrentavir
NS3-4A protease inhibitor (end with PREVIR)	Simeprevir Paritaprevir (ritonavir boosted) Grazoprevir Glecaprevir Voxilaprevir

Sofosbuvir (Solvaldi) (nucleotide analogue inhibitor of the HCV NS5B polymerase) – pan-genotypic
Taken with or without food
80% renally excreted – avoid if eGFR < 30
Enzyme inducers e.g Rifampicin, Carbamazepine etc will decrease effectiveness
Potentially life threatening bradycardia with Amiodarone (long t1/2 of amiodarone, means must be stopped for 3/12 pre sofosbuvir)
See www.hep-druginteractions.org to review all interactions

Administered with a NS5A inhibitor (Ledipasvir, Velpatasvir or Daclatasvir) – drugs that raise gastric pH will decrease their absorption; or with an NS5A inhibitor and NS2/4 protease inhibitor (Valpastasvir and Voxilaprevir) See www.hep-druginteractions.org to review all interactions.
Sofosbuvir + Ledipasvir (Harvoni), Sofosbuvir + Valpastasvir (Epclusa) and Sofosbuvir + Valpastasvir + Voxilaprevir (Vosevi) are all available as combined once daily tablet taken with and without food. Vosevi has the advantage of being a pangenotypic treatment.

Viekirax (Ombitasvir/ Paritaprevir/ Ritonavir) combines a NS5A inhibitor and protease inhibitor in a single tablet. Ritonavir inhibits metabolism of the protease inhibitor allowing for once daily dosing. It is given in combination with **Exviera (Dasabuvir)** ± Ribavirin in G1 infection and with Ribavirin alone in G4 infection.
Taken with food
It is metabolised by the liver and excreted in faeces. It can, therefore, be used in patients with renal impairment, but is contraindicated in Childs B and C cirrhosis.
Ritonavir is a potent inhibitor of cytochrome P450 mediated metabolism leading to several drug interactions. See www.hep-druginteractions.org to review all interactions.

Ribavirin - women of childbearing potential and/or their male partners must use an effective form of contraception during ribavirin-containing treatment and for a period of 6 months after the treatment has concluded. The dose of ribavirin should be adjusted downward by 200 mg at decrements if the haemoglobin level drops below 10 g/dl. Ribavirin administration should be stopped if the haemoglobin levels drops below 8.5 g/dl

Zepatier (Elbasvir/Grazoprevir) combines a NS5A inhibitor and protease inhibitor in a single tablet for use in G1 and G4 infection. Taken with and without food.
It is metabolised by the liver and excreted in faeces. It can, therefore, be used in patients with renal impairment, but is contraindicated in Childs B and C cirrhosis. Treatment length depends on whether the baseline viral load is > 800,000 IU/ml and/or on the results of resistance testing for NS5A polymorphisims.
See www.hep-druginteractions.org to review all interactions.

Maviret (Pibrentasvir/Glecaprevir) is a pangenotypic NS5A inhibitor and protease inhibitor.
Taken with food
No dose adjustment required in patients with renal impairment, but not recommended in patients with Childs B or C cirrhosis
See www.hep-druginteractions.org to review all interactions

Further reading:
EASL clinical practice guidelines - Management of HCV infection 2016. J Hep 2017; (66): 153-194

Documentation Controls

Development of Guideline:	Dr Adam Lawson
Consultation with:	Hepatology consultant and specialist nurse team
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Key Contact:	Dr Adam Lawson