Clinical Practice Guidelines

Hepatitis C Virus (HCV)

OBJECTIVE

The purpose is to guide the appropriate diagnosis and management of Hepatitis C Virus (HCV).

GUIDELINE

These are only guidelines, and are based on the best available information at the time. These may not be “all inclusive” as new medications and treatments are ever-evolving. These guidelines are updated by MDwise at least biannually or as national guidelines are updated.

Notice: Guidance for hepatitis C treatment in adults is changing constantly with the advent of new therapies and other developments. You should frequently review the guidance on the AASLD-IDSA website at: www.hcvguidelines.org for the latest recommendations.

ASSESSMENT AND DIAGNOSIS

Screening and Risk Assessment:

- One-time screening for HCV is recommended for persons born from 1945 through 1965 without prior ascertainment of risk
- Other persons should be screened for HCV infection risk factors. One-time testing should be performed for all persons with behaviors, exposures and conditions or circumstances associated with an increased risk of HCV
- Risk factors include:
  - Intranasal illicit drug use
  - Intravenous drug users
- Risk Exposures include:
  - Persons on long term hemodialysis
  - Persons with percutaneous and/or parenteral exposures in an unregulated setting
  - Healthcare, emergency medical, and public safety workers after needle-stick, sharps, or mucosal exposures to HCV-infected blood
  - Children born to HCV-infected women
  - Prior recipients of transfusions or organ transplants, including persons who:
- Were notified that they received blood from a donor who later tested positive for HCV
- Received a transfusion of blood or blood components, or underwent a living solid organ transplant before July 1992
- Received clotting factor concentrates produced before 1987
  - Persons who were ever incarcerated, Individuals who live or receive medical care in a high-prevalence setting (defined as a geographic location, or community with an HIV seroprevalence of at least 1%)
- Other conditions and circumstances:
  - HIV infection
  - Sexually active persons about to start pre-exposure prophylaxis (PreP) for HIV
  - Solid organ donors (deceased and living)
  - Unexplained chronic liver disease and/or chronic hepatitis, including elevated alanine aminotransferase (ALT) levels
- Annual HCV testing is recommended for persons who inject drugs and HIV-infected men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for HCV exposure

**Screening Tests**
- An HCV-antibody test is recommended for initial HCV testing. If the result is positive, current infection should be confirmed by a sensitive HCV-RNA test
- Among persons with a negative HCV-antibody test who are suspected of having liver disease, testing for HCV RNA or follow-up testing for HCV antibody is recommended if exposure to HCV occurred within the past 6 months; testing for HCV RNA can also be considered for persons who are immunocompromised
- Among persons at risk of reinfection after previous spontaneous or treatment-related viral clearance, initial HCV-RNA testing is recommended because an HCV-antibody test is expected to be positive
- Quantitative HCV-RNA testing is recommended prior to initiation of antiviral therapy to document the baseline level of viremia (i.e., baseline viral load)
- HCV genotype testing is recommended to guide selection of the most appropriate antiviral therapy
- Persons found to have a positive HCV-antibody test and negative results for HCV RNA by polymerase chain reaction (PCR) should be informed that they do not have evidence of current (active) HCV infection
HCV antibody test

Non-reactive
No HCV antibody detected
Stop

Reactive
HCV RNA Test
Current HCV Infection
Link to care
Not detected
No current HCV Infection
Counseling for Active HCV Persons:

- All patients with current HCV infection should receive education and interventions focused on reducing liver disease progression and preventing transmission of HCV.
- Alcohol abstinence and interventions are recommended.
- Screen for other conditions that may accelerate liver fibrosis, including Hepatitis B and HIV infections.
- Evaluations for advanced fibrosis using a liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection to assist in making appropriate HCV treatment strategies and to access the need for further interventions for cirrhosis management.
- Vaccinations for Hepatitis A and B is recommended for all patients susceptible to HCV infections.
- Vaccination for Pneumococcal infections is recommended for all patients with cirrhosis.
- All HCV patients should be educated about how to avoid transmitting the infection to others that include not sharing toothbrushes and dental or shaving equipment and being careful to cover any bleeding injuries or wounds.
- Patients should be advised to stop using illicit drugs and consider treatment for abuse. If drug use is continued, patients need to be advised to not reuse or share syringes, needles, water, cotton, or other drug preparation equipment.
- Always use new syringes, filters and disinfected cookers.
- Cleanse the injection site with a new alcohol swab with each use.
- Dispose of syringes and needles after one use in a safe puncture proof container.
- Patients with HCV should be advised not to donate blood and discuss HCV serostatus prior to donation of body organs, tissues or semen.
- Any surfaces and implements contaminated with visible blood from any HCV patients should be cleaned with a solution using a dilution of 1-part household bleach to 9 parts water and gloves should be worn when cleaning up blood spills.
- Patients with HIV infection and those with multiple sexual partners or other STD should be encouraged to use barrier precautions to prevent sexual transmission.
- All patients with a diagnosis of active HCV should be linked to a clinician who is able to provide comprehensive care management.

Other Testing preformed prior to ART treatment:

- Staging of hepatic fibrosis is essential before beginning treatment of HCV.
- Assessment of drug to drug interactions is recommended before beginning antiviral therapy.
- The following lab tests should be performed within 12 weeks prior to starting antiviral therapy:
  - Complete blood count
  - International normalized ratio (INR)
  - Hepatic function panel including albumin, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels
  - Calculated glomerular filtration rate (eGFR)
- HCV genotype and subtype as well as quantitative HCV RNA (HCV viral load) are recommended any time prior to treatment and used to guide treatment.
- In patients scheduled to receive an HCV NS3 protease inhibitor should be assessed for a history of decompensated liver disease and for liver disease severity using the Child-Turcotte-Pugh (CTP) score:
  - Patients with current or history of decompensated liver disease or with a current CTP score of ≥7.
should not receive treatment regimens that contain NS3 protease inhibitors due to increased blood levels and/or lack of safety data.

- Patients with a CTP score of 5 or 6 who cannot be closely monitored with labs or clinical symptoms during treatment should not receive paritaprevir/ritonavir.

- All patients initiating HCV direct-acting antiviral (DAA) therapy should be screened for HBV coinfection with HBsAg testing and for prior infection with anti-HBs and anti-HBc testing.

### Severity of Cirrhosis

| Child-Turcotte-Pugh (CPT Classification of the severity of Cirrhosis) |
|---------------------------|-------------------|-------------------|
| Factor | CLASS A | CLASS B | CLASS C |
| Total Points | 5 - 6 | 7 - 9 | 10 - 15 |
| Total bilirubin (µmol/L) | <34 | 34 - 50 | >50 |
| Serum albumin (g/L) | >35 | 28 - 35 | <28 |
| Prothrombin time / international national ratio (INR) | <1.7 | 1.71 - 2.3 | >2.3 |
| Ascites | None | Mild | Moderate to Severe |
| Hepatic encephalopathy | None | Grade I - II (or suppressed with medication) | Grade III - IV (or refractory) |

### On-treatment Monitoring

- Patients need to be educated about the medication regimen they will be placed on and education needs to include dosing, frequency of medications, food effects, missed doses, adverse effects with an emphasis placed on medication adherence, and the need for close supervision and blood testing during and after treatment.

- Clinic visits and/or telephone contact are recommended as clinically indicated to assure medication adherence during treatment, and to monitor adverse events and potential drug to drug interactions with prescribed medications.

- CBC, creatinine level, eGFR, and hepatic function panel is recommended after 4 weeks of treatment and as clinically indicated.

- More frequent monitoring for drug related adverse effects are recommended as clinically indicated (e.g., CBC for patients on ribavirin).

- A 10 fold increase in alanine aminotransferase (ALT) activity any time during the treatment should trigger discontinuation of therapy. While an increase in ALT < 10 fold that includes weakness, nausea, vomiting, jaundice or a significant rise in bilirubin, alkaline phosphatase or INR should also trigger discontinuing the treatment. Asymptomatic increases in ALT <10 fold should be monitored closely with ongoing monitoring of test at 2-week intervals. If the levels are still elevated, consideration should be given on discontinuing treatment.
Quantitative HCV viral load testing is recommended after 4 weeks of treatment and at 12 weeks post treatment. Antivirals should not be interrupted or discontinued if HCV RNA levels are not performed or available during treatment.

Post-Treatment Monitoring for Whom Treatment Failed to Reach a Sustained Virologic Response (SVR)
- Assessment of disease progression every 6-12 months with CBC, INR and hepatic function panel is recommended
- Screening for hepatocellular carcinoma using ultrasound every 6 months is recommended for all patients with advanced fibrosis
- Endoscopic screening for esophageal varices if cirrhosis is present is recommended
- Evaluation for retreatment should be considered as new effective alternatives are made available

Post-Treatment Monitoring for Whom Treatment Reach a Sustained Virologic Response
- In patients who do not have advanced fibrosis follow-up is the same as if they were never infected with HCV
- Assessment for HCV recurrence or reinfecion is recommended only if the patient has ongoing risk for HCV or another unexplained hepatic dysfunction occurs. In these instances, it is recommended that qualitative HCV RNA test be performed instead of HCV-antibody test to assess for recurrent or reinfecion of HCV
- Screening for hepatocellular carcinoma using ultrasound every 6 months is recommended for all patients with advanced fibrosis who reach SVR
- If cirrhosis is present a baseline endoscopy for varices is recommended. Those identified with varices should be treated and followed as indicated
- Other causes of liver diseases should be assessed for patients that develop persistently abnormal liver tests after achieving SVR

TREATMENT

While the antiviral therapy for chronic HCV infection is continuing to evolve, the goal of treatment of HCV patients is to decrease all-cause mortality and liver-related adverse effects, including end-stage liver disease, cirrhosis, and hepatocellular carcinoma, by achieving a virologic cure as evidenced by a sustained virologic response. Treatment is recommended for all patients with chronic HCV, except those with limited life expectancy that cannot be corrected with HCV treatment, liver transplant, or other directed therapies. These patients should be supervised in consultation with an expert.

Prior Authorization is required for treatment of HCV infection through OPTUMRx for the state of Indiana. For additional information on prior authorization for covered medications, please visit https://inm-providerportal.optum.com/. Hepatitis C Agents PA criteria can be found at the dropdown under Preferred Products > Pharmacy Criteria and Forms.
REFERENCES

AASLD-IDSA. HCV testing and linkage to care. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org/ Last reviewed 4/10/18

Clinical summary: Hepatitis C


Hepatitis C FAQs for health professionals. Centers for Disease Control and Prevention, Division of Viral Hepatitis website. www.cdc.gov/hepatitis/HCV/HCVfaq.htm Updated 4/30/18. Last access 4/10/18

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