Chronic HCV Infection: Pre-treatment Assessment Guide

This brochure contains recommendations from the AASLD and IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. See Guidelines for complete recommendations. AASLD is a registered trademark of the American Association for the Study of Liver Diseases, and IDSA is a registered trademark of the Infectious Diseases Society of America. AASLD and DSA have not endorsed, and are not sponsors of, or otherwise affiliated with this brochure by AbbVie Inc. All information subject to change.
Overview of Pre-treatment Workup

**Screening**
Who should be screened for HCV infection?

- All adults aged 18 years and older

- HCV antibody test

**Diagnosis**

- HCV RNA test

- HCV RNA detected

- HCV RNA not detected

**Potential Assessments**

- Laboratory workup
  - HCV genotype
  - CBC with platelets
  - Hepatic function panel
  - HIV coinfection
  - HBV coinfection
  - eGFR • CMP • INR
  - Resistance-associated substitutions

- Assessment for advanced fibrosis/cirrhosis
  - FIB-4
  - APRI
  - FibroSure®
  - FibroScan®

- Additional considerations
  - Age
  - Pregnancy
  - Prior HCV treatment history
  - Immunization history
  - Medical or psychiatric comorbidities
  - Concomitant medications
  - Injection drug use
  - Patient readiness
  - Patient counseling/education

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FibroSure® is a registered trademark of Laboratory Corporation of America Holdings.
FibroScan® is a registered trademark of Echosens Company.
Who Should Be Screened for HCV Infection?

In the United States, approximately 2.3 million adults are infected with HCV. Approximately 50% of people with HCV do not know they are infected; therefore, all adults and individuals with known risk factors are recommended for HCV screening.

One-time testing for HCV infection is recommended for:

- All individuals aged 18 years and older

Periodic repeat HCV testing & One-time HCV testing (individuals aged less than 18 years) should be offered to persons with the following:

**Risk behaviors**
- Current or former injection drug users (including those who only injected once)
  - Annual testing recommended for current injection drug users
- Persons with intranasal illicit drug use
- Men who have sex with men

**Risk exposures**
- Persons who were ever incarcerated
- Persons who were ever on long-term hemodialysis
- Persons who have had percutaneous/parenteral exposures in an unregulated setting (eg, tattoos received outside of licensed parlors)
- Healthcare, emergency medical, and public safety workers after needle stick, sharps, or mucosal exposures to HCV-positive blood
- Children born to HCV-positive 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 infection
  - Received a transfusion of blood, blood components, or an organ transplant before July 1992
  - Received clotting factor concentrates produced before 1987

**Other conditions and circumstances**
- Persons who have HIV infection
  - Annual testing recommended for men with HIV who have unprotected sex with men
- Sexually active persons about to start PreP for HIV
- Persons with unexplained chronic liver disease and/or chronic hepatitis, including elevated ALT levels
- Persons who are solid organ donors (deceased and living) and solid organ transplant recipients

For more information regarding the epidemiology of HCV, see: [MappingHepC.com](http://MappingHepC.com)
**Screening and Diagnosis**

**How Is HCV Infection Diagnosed?**

**Recommended Testing Sequence:**

1. **HCV antibody test**
   - Detects HCV antibodies
   - **Reactive**
     - Does not distinguish between past exposure or current infection, means that the person was infected at some point in time
   - **Not detected**
     - No current HCV infection
     - No action required in most cases
   - **Non-reactive**
     - No HCV antibody detected
     - No exposure

2. **Check HCV RNA in individuals who:1,4**
   - Are immunocompromised (e.g., receiving chronic hemodialysis)
   - Might have been exposed to HCV within the past 6 months

3. **Retesting for HCV RNA in a subsequent blood sample, at least 6 months after the initial RNA test, is recommended to confirm chronic infection**

**Reflex Testing:**

- Diagnosis can be facilitated by automatically testing for HCV RNA on the same sample if the HCV antibody test is positive.

**HCV antibody test with reflex to quantitative HCV RNA test:**

- **CPT code:** 868038
- **Quest Diagnostics™ code:** 84729
- **LabCorp code:** 14405010

**Link to care and appropriate counseling**
Assessment

**What Laboratory Assessments Should Be Considered After Chronic HCV Diagnosis?**

Laboratory workup is recommended before a treatment is chosen.¹

**Recommended Laboratory Tests¹**

<table>
<thead>
<tr>
<th>CBC with platelets</th>
<th>Hepatic function panel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Albumin, total and direct bilirubin, ALT, AST</td>
</tr>
<tr>
<td>HIV</td>
<td>INR</td>
</tr>
<tr>
<td>eGFR</td>
<td>CMP</td>
</tr>
<tr>
<td>Resistance-associated substitutions*</td>
<td></td>
</tr>
</tbody>
</table>

**HBV Testing¹²¹¹**
- HBV reactivation during/after DAA therapy has been reported in HBV/HCV-coinfected patients (not receiving HBV suppressive therapy). Some cases have resulted in fulminant hepatitis, hepatic failure, and death
- Test all patients for evidence of current or prior HBV infection before initiating treatment with DAAs

**Interpretation of Results¹²¹³**

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>Susceptible to HBV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vaccinate for HBV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>Immune due to HBV immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Continue with pretreatment assessments</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>Immune due to natural infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Check HBV DNA, anti-HBc immunoglobulin M, and HBV e-antigen</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>Infected with HBV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider referring to a specialist for care</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>Interpretation unclear, four possibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1. Resolved infection (most common); 2. False-positive anti-HBc, susceptible; 3. &quot;Low level&quot; chronic infection; 4. Resolving acute infection</td>
</tr>
</tbody>
</table>

*Recommended for select DAA treatments.*¹

**HCV Genotyping¹²**

There are six common HCV genotypes:

**GT1** is the most prevalent in the United States¹⁴

**HCV genotyping** may be considered for those in whom it may alter treatment recommendations

**HCV genotyping:**

CPT code: 87902² | Quest Diagnostics™ code: 37811¹⁵ | LabCorp code: 550475¹⁶
The staging of hepatic fibrosis is key to determining the initial and follow-up management of patients. Several assessments for fibrosis are recommended, including liver biopsy, imaging, and/or non-invasive tests.

### Overview of Non-invasive Liver Fibrosis Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
<th>Formula</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>In a Population with a Cirrhosis Prevalence of 15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIB-4</td>
<td>A quantitative method to estimate the risk of advanced liver disease</td>
<td>Age (years) x AST (U/L) / Platelet count (10^9/L) x √ALT (U/L)</td>
<td>55% sensitivity</td>
<td>92% specificity</td>
<td>FIB-4 &lt;1.45 is 97% predictive of not having cirrhosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>90% sensitivity</td>
<td></td>
<td>FIB-4 &gt;1.45 is 97% predictive of having cirrhosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>58% specificity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibrosis severity correlates with ↑ in AST level and ↓ in platelet count</td>
<td></td>
<td>77% sensitivity</td>
<td>75% specificity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>APRI</td>
<td>AST level (IU/L) / AST (upper limit of normal) (IU/L)</td>
<td>55% sensitivity</td>
<td>92% specificity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Platelet count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>90% sensitivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>58% specificity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FibroSure®</td>
<td>A quantitative method to estimate level of liver scarring</td>
<td>Calculated using six biochemical serum markers, age, and gender</td>
<td>85% sensitivity</td>
<td>74% specificity</td>
<td>In a population with a cirrhosis prevalence of 15%, FibroSure® &lt;0.56 is 97% predictive of not having cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Commercially available test (available online)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>CPT code: 550123</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quest Diagnostic™ code: 92688™</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LabCorp code: 550123</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>FibroScan®</td>
<td>A non-invasive device to estimate degree of hepatic fibrosis</td>
<td>87% sensitivity</td>
<td>91% specificity</td>
<td>In a population with a cirrhosis prevalence of 15%, FibroScan® &lt;12.5 is 98% predictive of not having cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Measures liver stiffness using transient elastography</td>
<td></td>
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<tr>
<td></td>
<td>Requires ultrasound evaluation: the more rapid the ultrasound wave spreads, the stiffer the liver (expressed in kilopascals)</td>
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</tr>
<tr>
<td></td>
<td>CPT code: 91200</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quest Diagnostic™ code: 92688™</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>LabCorp code: 550123</td>
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<td></td>
</tr>
</tbody>
</table>

### Liver Fibrosis Progression in Patients With Chronic HCV

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Annual Risk of HCC</th>
<th>Annual Risk of Hepatic Decompensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>No fibrosis, portal fibrosis without septa</td>
<td>1–5%</td>
<td></td>
</tr>
<tr>
<td>F1</td>
<td>Minimal fibrosis, F1, portal fibrosis without septa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F2</td>
<td>Moderate fibrosis, F2, few septa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F3</td>
<td>Advanced fibrosis, F3, numerous septa without cirrhosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F4</td>
<td>Cirrhosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCC</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Child-Pugh Classification of the Severity of Cirrhosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Points</th>
<th>Ascites</th>
<th>Hepatic encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>No fibrosis, portal fibrosis without septa</td>
<td>0</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>F1</td>
<td>Minimal fibrosis, F1, portal fibrosis without septa</td>
<td>1</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>F2</td>
<td>Moderate fibrosis, F2, few septa</td>
<td>2</td>
<td>Mild</td>
<td>Grade I–II (or suppressed with medication)</td>
</tr>
<tr>
<td>F3</td>
<td>Advanced fibrosis, F3, numerous septa without cirrhosis</td>
<td>3</td>
<td>Moderate to severe</td>
<td>Grade III-IV (or refractory)</td>
</tr>
</tbody>
</table>

*See online calculators for Child-Pugh score.
### Assessment

**What Else Should Be Considered Prior to Treatment?**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Consult DAA products’ prescribing information for age-related dosing considerations.</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>Antiviral therapy is recommended before pregnancy, wherever practical and feasible. See AASLD–IDSA guidelines for further considerations.</td>
</tr>
<tr>
<td><strong>Prior HCV Treatment History</strong></td>
<td>Prior HCV treatment is a factor in choosing the antiviral regimen and appropriate dosing regimen. Consult AASLD–IDSA guidelines and DAA products’ prescribing information for further information.</td>
</tr>
<tr>
<td><strong>Immunization History</strong></td>
<td>Vaccination against HAV and HBV is recommended for all susceptible persons with HCV. Vaccination against pneumococcal infection is recommended for all patients with cirrhosis.</td>
</tr>
<tr>
<td><strong>Presence of Medical or Psychiatric Comorbidities</strong></td>
<td>Medical and psychiatric comorbidities can be considered a barrier to treatment. Refer to AASLD–IDSA guidelines for recommendations on how to manage these in patients with HCV infection.</td>
</tr>
<tr>
<td><strong>Use of Concomitant Medications</strong></td>
<td>There are potential drug–drug interactions. Consult AASLD–IDSA guidelines and DAA products’ prescribing information for guidance on how to manage these.</td>
</tr>
<tr>
<td><strong>Injection Drug Use</strong></td>
<td>Active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment.</td>
</tr>
</tbody>
</table>
| **Patient Readiness** | It is important to ensure that patients are ready to engage effectively in their treatment by:  
  - Assessing the potential barriers to treatment  
  - Supporting patients through referral to appropriate services and programs, such as harm reduction services and needle/syringe service programs for persons who inject drugs  
  - Educating patients about actions that can be taken to protect liver health  
  - Providing resources for treatment adherence (eg, pill pots and medication reminders) |
| **Patient Counseling/Education** | In addition to antiviral treatment, counseling and education for patients is recommended:  
  - Avoidance of HCV transmission  
  - Guidance on partner and household testing  
  - Interventions to reduce liver disease progression:  
    - Awareness of conditions that may accelerate liver fibrosis, including metabolic syndrome/diabetes and obesity  
    - Avoidance of new medicines (including over-the-counter and herbal agents) without first checking with a healthcare provider  
    - Abstinence from alcohol (and interventions to facilitate this where appropriate) |
References


Diagnosis and Test Codes

ICD-10 Diagnosis Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B17.1</td>
<td>Acute hepatitis C</td>
</tr>
<tr>
<td>B18.2</td>
<td>Chronic hepatitis C</td>
</tr>
</tbody>
</table>

HCV antibody test with reflex to quantitative HCV RNA test:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>89803</td>
<td>CPT code: 89803</td>
</tr>
<tr>
<td>9472</td>
<td>Quest Diagnostics™ code: 8472</td>
</tr>
<tr>
<td>144050</td>
<td>LabCorp code: 144050</td>
</tr>
</tbody>
</table>

HCV genotyping:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>87902</td>
<td>CPT code: 87902</td>
</tr>
<tr>
<td>37811</td>
<td>Quest Diagnostics™ code: 37811</td>
</tr>
<tr>
<td>550475</td>
<td>LabCorp code: 550475</td>
</tr>
</tbody>
</table>

FibroSure®:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81596</td>
<td>CPT code: 81596</td>
</tr>
<tr>
<td>92866</td>
<td>Quest Diagnostics™ code: 92866</td>
</tr>
<tr>
<td>550123</td>
<td>LabCorp code: 550123</td>
</tr>
</tbody>
</table>

FibroTest®:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>91200</td>
<td>CPT code: 91200</td>
</tr>
</tbody>
</table>

AASLD
American Association for the Study of Liver Diseases

ALT
Alanine aminotransferase

Anti-HBc
Antibody to hepatitis B core antigen

Anti-HBs
Antibody to hepatitis B surface antigen

APRI
AST to Platelet Ratio Index

AST
Aspartate aminotransferase

CBC
Complete blood count

CDC
Centers for Disease Control and Prevention

CPT
Current procedural terminology

DAAS DIRECT-ACTING ANTIVIRALS

eGFR
Estimated glomerular filtration rate

FDA
US Food and Drug Administration

Fib-4
Fibrosis-4

GT
Genotype

HAV
Hepatitis A virus

HBsAg
Hepatitis B surface antigen

HBV
Hepatitis B virus

HCC
Hepatocellular carcinoma

HCV
Hepatitis C virus

HIV
Human immunodeficiency virus

IDSA
Infectious Diseases Society of America

INR
International normalized ratio

IU/L
International units per liter

PCR
Polymerase chain reaction

PreP
Pre-exposure prophylaxis

RNA
Ribonucleic acid