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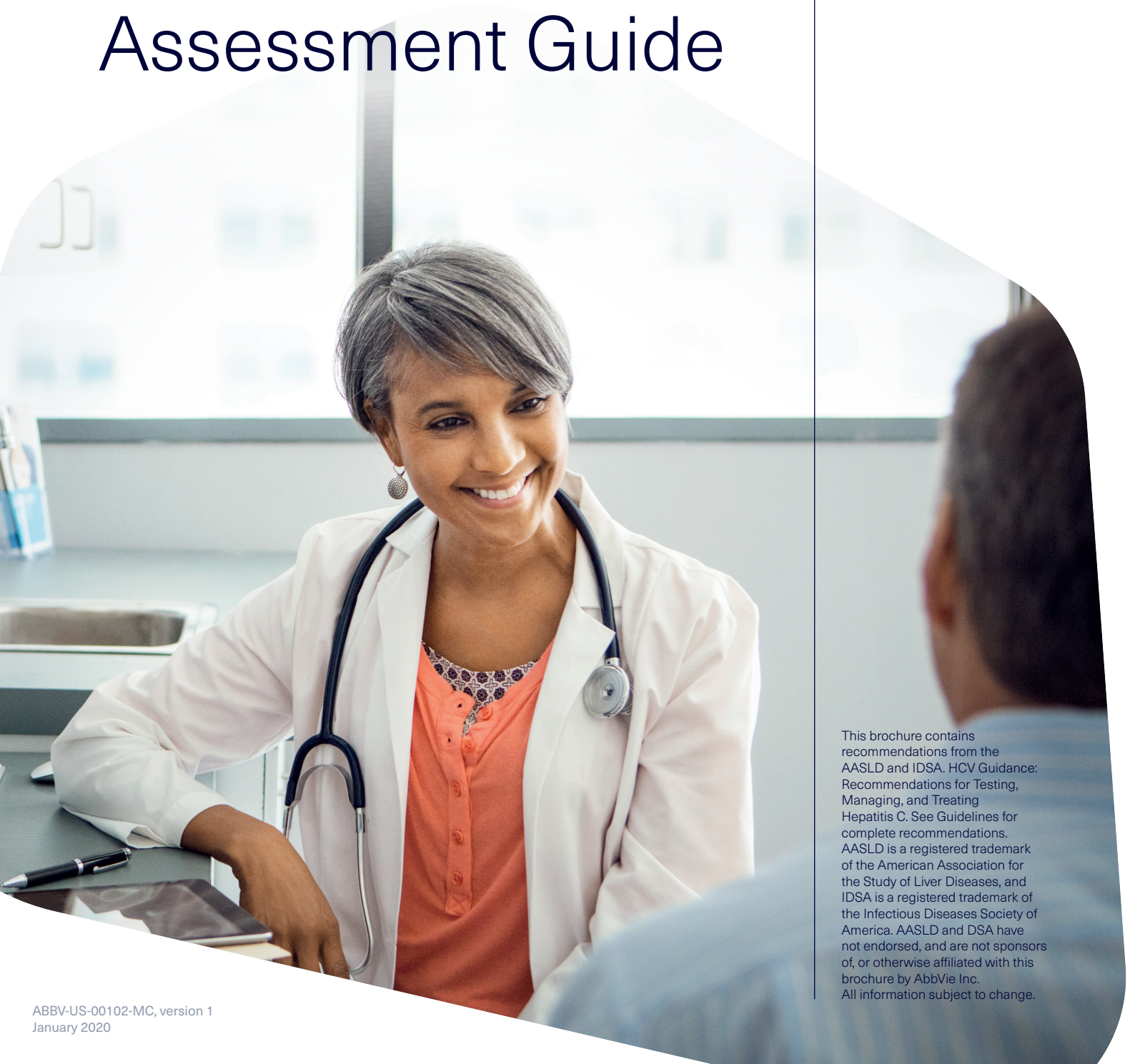
Chronic HCV Infection:

Pre-treatment Assessment Guide



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Overview of Pre-treatment Workup

Screening[1–4]

Who should be screened for HCV infection?

All adults aged 18 years and older

HCV antibody test

Reactive

Non-reactive

Diagnosis[1–4]

HCV RNA test

HCV RNA detected

HCV RNA not detected

Potential Assessments[1,2]

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

Screening

Who Should Be Screened for HCV Infection?

In the United States, approximately

2.3 million

adults are infected with HCV.[5] Approximately 50% of people with HCV do not know they are infected[6]; therefore, all adults and individuals with known risk factors are recommended for HCV screening.[1–3]

For more information regarding the epidemiology of HCV, see:

MappingHepC.com

One-time testing for HCV infection is recommended for:[1–3]

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:[1]

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

Other conditions and circumstances

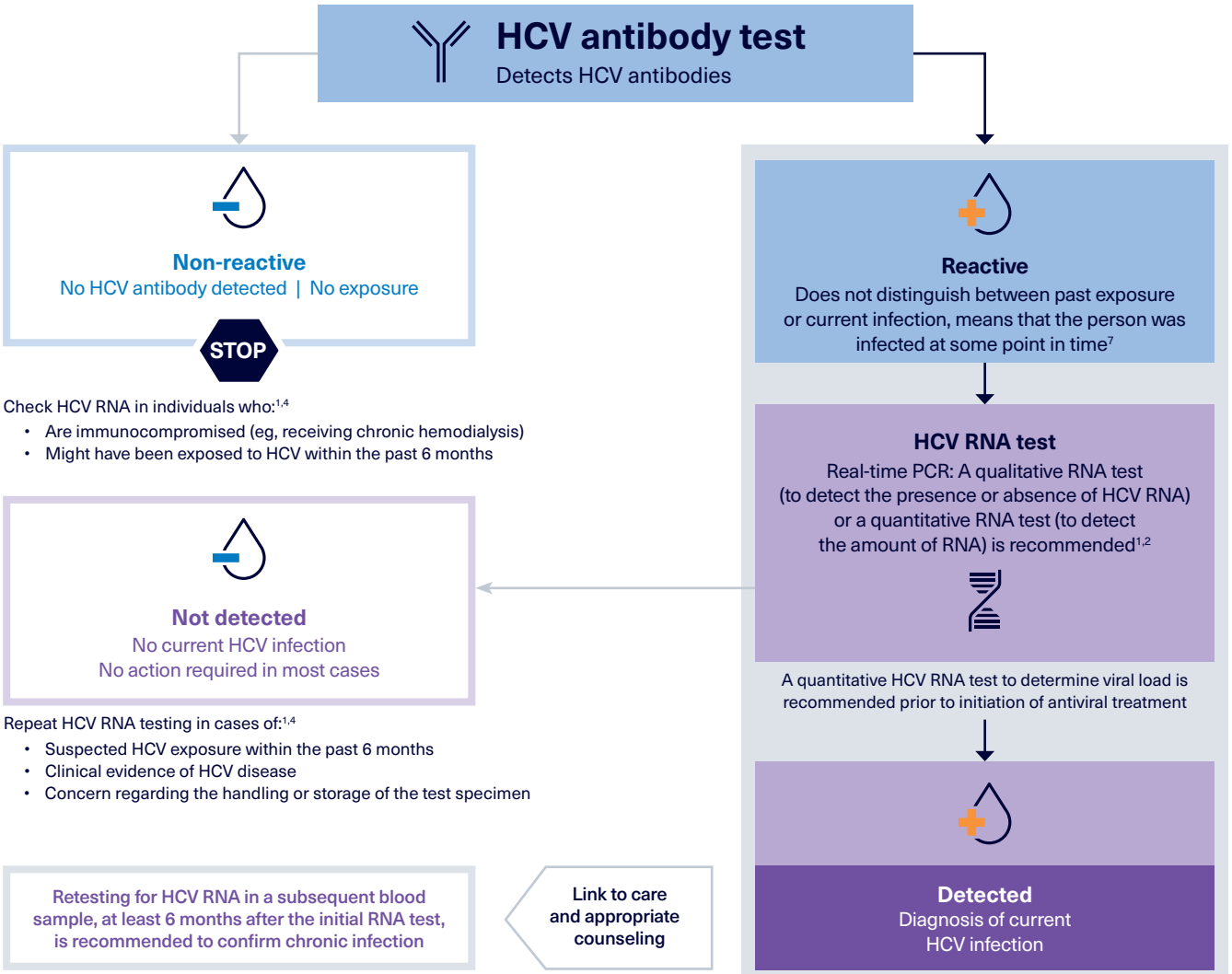
- Persons who have HIV infection
  - *Annual testing recommended for men with HIV who have unprotected sex with men*
- Sexually active persons about to start PreP for HIV
- Persons with unexplained chronic liver disease and/or chronic hepatitis, including elevated ALT levels
- Persons who are solid organ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

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

How Is HCV Infection Diagnosed?

Recommended Testing Sequence:[1,4]



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: 86803[8] | Quest Diagnostics™ code: 8472[9] | LabCorp code: 144050[10]

Assessment

What Laboratory Assessments Should Be Considered After Chronic HCV Diagnosis?

Laboratory workup is recommended before a treatment is chosen.[1]

Recommended Laboratory Tests[1]

CBC with platelets	Hepatic function panel Albumin, total and direct bilirubin, ALT, AST	HIV	INR	eGFR	CMP	Resistance-associated substitutions*

HBV Testing[1,2,11]

- 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 Results[12,13]

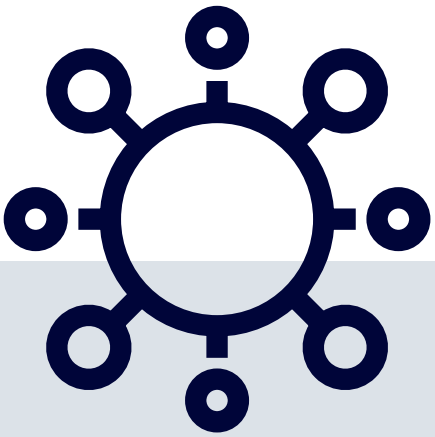
HBsAg	Anti-HBc	Anti-HBs	
−	−	−	**Susceptible to HBV infection** Vaccinate for HBV
−	−	+	**Immune due to HBV immunization** Continue with pretreatment assessments
−	+	+	**Immune due to natural infection** Check HBV DNA, anti-HBc immunoglobulin M, and HBV e-antigen
+	+	−	**Infected with HBV** Consider referring to a specialist for care
−	+	−	**Interpretation unclear, four possibilities** **1.** Resolved infection (most common); **2.** False-positive anti-HBc, susceptible; **3.** "Low level" chronic infection; **4.** Resolving acute infection

*Recommended for select DAA treatments.[1]

HCV Genotyping[1,2]

There are six common HCV genotypes:

GT1 is the most prevalent in the United States[14]



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

HCV genotyping:

CPT code: 87902[8] | Quest Diagnostics™ code: 37811[15] | LabCorp code: 550475[16]

How Is Fibrosis Assessed?

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.[1]

Overview of Non-invasive Liver Fibrosis Tests*

FIB-4[17–19]

A quantitative method to estimate the risk of advanced liver disease

$$\frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

FIB-4 >1.45
- 90% sensitivity
- 58% specificity

FIB-4 >3.25
- 55% sensitivity
- 92% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%:
- FIB-4 <1.45 is 97% predictive of not having cirrhosis
- FIB-4 <3.25 is 92% predictive of not having cirrhosis

APRI[17,19,20]

A quantitative method to predict presence of fibrosis/cirrhosis

$$\frac{\dfrac{\text{AST level (IU/L)}}{\text{AST (upper limit of normal}^{\dagger}\text{) (IU/L)}}}{\text{Platelet count}}$$

†Usually 40 IU/L

Fibrosis severity correlates with ↑ in AST level and ↓ in platelet count

APRI >1
- 77% sensitivity
- 75% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%, APRI ≤1 is 95% predictive of not having cirrhosis

FibroSure®[17,20–22]

A quantitative method to estimate level of liver scarring
- Calculated using six biochemical serum markers, age, and gender

Score ranges from 0.00–1.00
- Corresponds to fibrosis stages F0–F4

Commercially available test (available online)
- Test code: 550123

FibroSure® >0.56
- 85% sensitivity
- 74% specificity

for predicting cirrhosis

In a population with a cirrhosis prevalence of 15%, FibroSure® <0.56 is 97% predictive of not having cirrhosis

CPT code: 81596[23] | Quest Diagnostic™ code: 92688[24] | LabCorp code: 550123[25]

FibroScan®[17,21,22,26]

Non-invasive device to estimate degree of hepatic fibrosis
- Measures liver stiffness using transient elastography
- Requires ultrasound evaluation: the more rapid the ultrasound wave spreads, the stiffer the liver (expressed in kilopascals)

FibroScan® >12.5
- 87% sensitivity
- 91% specificity

for predicting cirrhosis

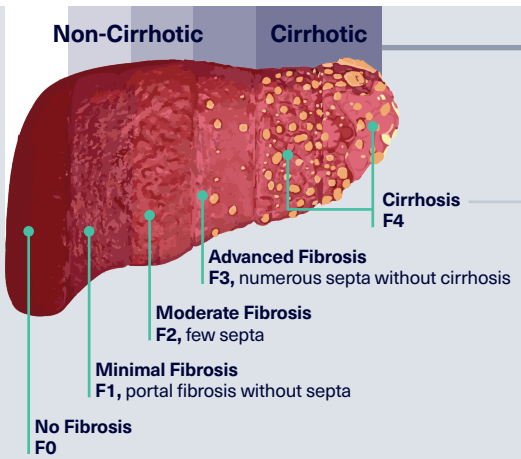
In a population with a cirrhosis prevalence of 15%, FibroScan® <12.5 is 98% predictive of not having cirrhosis

CPT code: 91200[27]

*Does not include all tests for fibrosis; online calculators are available for FIB-4 and APRI score.

Advanced fibrosis/cirrhosis require long-term follow-up with a specialist and HCC screening.
HCC screening with ultrasound is recommended every 6 months in patients with advanced fibrosis/cirrhosis regardless of treatment outcome.[1]

Liver Fibrosis Progression in Patients With Chronic HCV[1,2,28]



1–5%
annual risk of HCC (in patients with cirrhosis)

Child-Pugh A (5–6 points)
Compensated cirrhosis

Child-Pugh B (7–9 points)
Child-Pugh C (10–15 points)
Decompensated cirrhosis

Patients require close monitoring and should be treated by experienced physicians.[1]
Not all FDA-approved treatments for chronic HCV infection are indicated in patients with Child-Pugh B/C.

3–6%
annual risk of hepatic decompensation (in patients with cirrhosis)

Child-Pugh Classification of the Severity of Cirrhosis[1‡]

Factor	Total bilirubin (mg/dL)	Serum albumin (g/L)	INR	Ascites	Hepatic encephalopathy
1 point	<2	>35	<1.7	None	None
2 points	2–3	28–35	1.71–2.3	Mild	Grade I–II (or suppressed with medication)
3 points	>3	<28	>2.3	Moderate to severe	Grade III–IV (or refractory)

‡Online calculators are available for Child-Pugh score.

What Else Should Be Considered Prior to Treatment?

Age

- Consult DAA products' prescribing information for age-related dosing considerations.

Pregnancy[1]

- Antiviral therapy is recommended before pregnancy, wherever practical and feasible. See AASLD–IDSA guidelines for further considerations.

Prior HCV Treatment History[1]

- 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.

Immunization History[1,2]

- Vaccination against HAV and HBV is recommended for all susceptible persons with HCV.
- Vaccination against pneumococcal infection is recommended for all patients with cirrhosis.

Presence of Medical or Psychiatric Comorbidities[1]

- 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.

Use of Concomitant Medications[1]

- There are potential drug–drug interactions. Consult AASLD–IDSA guidelines and DAA products' prescribing information for guidance on how to manage these.

Injection Drug Use[1]

- Active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment.

Patient Readiness[29]

- 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[1,2]

- 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)

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Diagnosis and Test Codes

ICD-10 Diagnosis Codes

Acute hepatitis C: B17.1 Chronic hepatitis C: B18.2

Test Codes

HCV antibody test with reflex to quantitative HCV RNA test:
- CPT code: 86803
- Quest Diagnostics™ code: 8472
- LabCorp code: 144050

HCV genotyping:
- CPT code: 87902
- Quest Diagnostics™ code: 37811
- LabCorp code: 550475

FibroSure®:
- CPT code: 81596
- Quest Diagnostic™ code: 92866
- LabCorp code: 550123

FibroTest®:
- CPT code: 91200

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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

CMP
Comprehensive metabolic panel

CPT
Current procedural terminology

DAA
Direct-acting antiviral

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