


HCV Testing and Linkage to Care

Recommendations for One-Time Hepatitis C Testing

| RECOMMENDED | RATING  |
|--|--|
| One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years or older. | I, B |
| One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below). | I, B |
| Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy. | I, B |
| Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below). | Ila, C |
| Annual HCV testing is recommended for all persons who inject drugs , for HIV-infected men who have unprotected sex with men , and men who have sex with men taking pre-exposure prophylaxis (PrEP) . | Ila, C |

Risk Activities

- Injection drug use (current or ever, including those who injected only once)
- Intranasal illicit drug use
- Use of glass crack pipes
- Male engagement in sex with men
- Engagement in chem sex (defined as the intentional combining of sex with the use of particular nonprescription drugs in order to facilitate or enhance the sexual encounter [[Bourne, 2015](#)])

Risk Exposures

- Persons on long-term hemodialysis (ever)
- Persons with percutaneous/parenteral exposures in an unregulated setting
- Healthcare, emergency medical, and public safety workers after needlestick, sharps, or mucosal exposure to HCV-infected blood
- Children born to HCV-infected women
- Recipients of a prior transfusion or organ transplant, 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 an organ transplant before July 1992
 - Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated


Other Conditions and Circumstances

Recommendations for One-Time Hepatitis C Testing

- HIV or HBV infection
- Sexually active persons about to start pre-exposure prophylaxis (PrEP) for HIV
- Chronic liver disease and/or chronic hepatitis, including unexplained elevated alanine aminotransferase (ALT) levels
- Solid organ donors (living and deceased) and solid organ transplant recipients


Initial HCV Testing and Follow-Up

Recommendations for Initial HCV Testing and Follow-Up

| RECOMMENDED | RATING  |
|--|--|
| HCV-antibody testing with reflex HCV RNA polymerase chain reaction (PCR) testing is recommended for initial HCV testing. | I, A |
| Among persons with a negative HCV-antibody test who were exposed to HCV within the prior 6 months, HCV-RNA or follow-up HCV-antibody testing 6 months or longer after exposure is recommended. HCV-RNA testing can also be considered for immunocompromised persons. | I, C |
| Among persons at risk of reinfection after previous spontaneous or treatment-related viral clearance, HCV-RNA testing is recommended because a positive HCV-antibody test is expected. | I, C |
| Quantitative HCV-RNA testing is recommended prior to initiation of antiviral therapy to document the baseline level of viremia (ie, baseline viral load). | I, A |
| HCV genotype testing may be considered for those in whom it may alter treatment recommendations. | I, A |
| Persons found to have a positive HCV-antibody test and negative results for HCV RNA by PCR should be informed that they do not have evidence of current (active) HCV infection but are not protected from reinfection. | I, A |

Counseling Persons With Active HCV Infection

Recommendations for Counseling Persons With Active HCV Infection


| RECOMMENDED | RATING  |
|---|--|
| Persons with current HCV infection should receive education and interventions aimed at reducing liver disease progression and preventing HCV transmission. | IIa, B |
| Abstinence from alcohol and, when appropriate, interventions to facilitate cessation of alcohol consumption should be advised for all persons with HCV infection. | IIa, B |
| Evaluation for other conditions that may accelerate liver fibrosis, including hepatitis B and HIV infections, is recommended for all persons with active HCV infection. | IIb, B |

Recommendations for Counseling Persons With Active HCV Infection

| | |
|--|--------|
| Evaluation for advanced hepatic fibrosis using noninvasive tests (serum panels, elastography) or liver biopsy, if required, is recommended for all persons with HCV infection to facilitate an appropriate decision regarding HCV treatment strategy, and to determine the need for initiating additional measures for cirrhosis management (eg, hepatocellular carcinoma screening) (see Monitoring section). | I, A |
| Vaccination against hepatitis A and hepatitis B is recommended for all susceptible persons with HCV infection. | IIa, C |
| Vaccination against pneumococcal infection is recommended for all patients with cirrhosis. | IIa, C |
| All persons with HCV infection should be provided education about how to prevent HCV transmission to others. | I, C |

Linkage to Care


Recommendation for Linkage to Care

| RECOMMENDED | RATING  |
|---|--|
| All persons with active HCV infection should be linked to a healthcare provider who is knowledgeable in and prepared to provide comprehensive management. | IIa, C |


Last update: October 24, 2022

When and in Whom to Initiate HCV Therapy


Goal of Treatment


| RECOMMENDED | RATING  |
|--|--|
| The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response. | I, A |

Recommendation for When and in Whom to Initiate Treatment

| RECOMMENDED | RATING  |
|---|--|
| Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. | I, A |

Pretreatment Assessment


| Recommendation for Pretreatment Assessment | |
|--|--|
| RECOMMENDED | RATING  |
| Evaluation for advanced fibrosis using noninvasive markers and/or elastography, and rarely liver biopsy, is recommended for all persons with HCV infection to facilitate decision making regarding HCV treatment strategy and determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see HCV Testing and Linkage to Care). | I, A |

| Recommendation for Repeat Liver Disease Assessment | |
|---|--|
| RECOMMENDED | RATING  |
| Ongoing assessment of liver disease is recommended for persons in whom therapy is deferred. | I, C |

Last reviewed: October 24, 2022

Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy

Pretreatment and On-Treatment Monitoring

| Recommended Assessments Prior to Starting DAA Therapy | |
|--|--|
| RECOMMENDED | RATING  |
| Staging of hepatic fibrosis is essential prior to HCV treatment (see Testing and Linkage to Care and see When and in Whom to Treat). | I, C |
| Assessment of potential drug-drug interactions with concomitant medications is recommended prior to starting DAA therapy and, when possible, an interacting co-medication should be stopped or switched to an alternative with less risk for potential interaction during HCV treatment. (See Table of Drug Interactions with Direct-Acting Antivirals and Selected Concomitant Medications below or use | |

Recommended Assessments Prior to Starting DAA Therapy

an online resource such as [University of Liverpool interaction checker](#).)

Patients should be educated about the proper administration of DAA medications (eg, dose, frequency of medicines, food effects, missed doses, adverse events, etc), the crucial importance of adherence, and the need to inform the healthcare provider about any changes to their medication regimen.

The following laboratory tests are recommended within 6 months prior to starting DAA therapy:

- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, serum albumin, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
- Estimated glomerular filtration rate (eGFR)

The following laboratory tests are recommended any time prior to starting DAA therapy:

- Quantitative HCV RNA (HCV viral load)
- If a nonpangenotypic DAA will be prescribed, then test for HCV genotype and subtype.

The safety of ribavirin-free DAA regimens in humans has not been established during pregnancy and for nursing mothers, so counseling should be offered to women of childbearing age before beginning HCV treatment. (See ribavirin pregnancy recommendations below.)

I, C

All patients initiating DAA therapy should be assessed for active hepatitis B virus (HBV) coinfection with HBV surface antigen (HBsAg) testing, and for evidence of prior infection with HBV core antibody (anti-HBc) and HBV surface antibody (anti-HBs) testing.

IIa, B

Patients found or known to be HBsAg-positive should be assessed for whether their HBV DNA level meets [AASLD criteria for HBV treatment and initiation of antiviral therapy for HBV](#).

Strong, Moderate^a

All patients should be assessed for HIV coinfection prior to initiating DAA therapy.

IIa, B

Testing for the presence of resistance-associated substitutions (RASs) prior to starting treatment should be performed as recommended in the [Initial Treatment](#) and the [Retreatment](#) sections. Additional information about RAS testing can be found in the [HCV Resistance Primer](#).

IIb, B


Patients scheduled to receive an HCV NS3 protease inhibitor (ie, grazoprevir, voxilaprevir, glecaprevir) should be assessed for a history of decompensated liver disease and liver disease severity using the Child-Turcotte-Pugh (CTP) score (see third-party calculator).

I, A

- Patients with current or prior history of decompensated liver disease or with a current CTP score ≥ 7 should **not** receive treatment with regimens that contain NS3 protease inhibitors due to increased blood levels and/or lack of safety data.


^a Unlike the AASLD/IDSA HCV guidance, the AASLD guidelines for treatment of chronic hepatitis B uses the GRADE system to rate recommendations; please see that [document](#) for further information about this rating system.

Recommended Monitoring During Antiviral Therapy


| RECOMMENDED | RATING  |
|--|--|
| Clinic visits or telephone contact are recommended as clinically indicated during treatment to ensure medication adherence and monitor for adverse events and potential drug-drug interactions (see table of Drug Interactions with Direct-Acting Antivirals and Selected Concomitant Medications below), especially with newly prescribed medications. | I, B |
| Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. On-treatment and posttreatment monitoring for hypoglycemia is recommended. | I, C |
| Inform patients taking warfarin of the potential for changes in their anticoagulation status. On-treatment and posttreatment INR monitoring for subtherapeutic anticoagulation is recommended. | I, C |
| Patients receiving elbasvir/grazoprevir should be monitored with a hepatic function panel at 8 weeks and again at 12 weeks if receiving 16 weeks of treatment. | I, B |
| <p>A ≥ 10-fold increase in ALT values from baseline at any time during treatment should prompt discontinuation of DAA therapy (especially with signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR).</p> <p>An increase in ALT < 10-fold from baseline that is accompanied by any weakness, nausea, vomiting, jaundice, or significantly increased bilirubin, alkaline phosphatase, or INR should also prompt discontinuation of DAA therapy.</p> <p>Asymptomatic increases in ALT < 10-fold from baseline should be closely monitored with repeat testing at 2-week intervals. If levels remain persistently elevated, consideration should be given to discontinuation of DAA therapy.</p> | I, B |
| Quantitative HCV viral load testing is recommended 12 or more weeks after completion of therapy to document sustained virologic response (SVR), which is consistent with cure of chronic HCV infection. | I, B |
| <p>For HBsAg-positive patients not already receiving HBV suppressive therapy because their baseline HBV DNA level does not meet treatment criteria, one of two approaches may be taken:</p> <ul style="list-style-type: none"> Initiate prophylactic HBV antiviral therapy for those with low or undetectable HBV DNA levels. If this course is elected, pending further data, prophylaxis should be continued until 12 weeks after completion of DAA therapy. Monitor HBV DNA levels monthly during and immediately after DAA therapy. Antiviral treatment for HBV should be given in the event of a rise in HBV DNA > 10-fold above baseline or to > 1000 IU/mL in those with a previously undetectable or unquantifiable HBV DNA level. | IIa, B |

Posttreatment Follow-Up for Patients in Whom Treatment Failed

Recommended Monitoring for Patients in Whom Treatment Failed to Achieve a Sustained Virologic Response


| RECOMMENDED | RATING  |
|--|--|
| Retreatment for chronic HCV is recommended utilizing the regimens recommended in the Retreatment section. | I, C |
| Disease progression assessment every 6 to 12 months with a hepatic function panel, complete blood count (CBC), and international normalized ratio (INR) is recommended if patients are not retreated or fail a second or third DAA treatment course. | I, C |
| Surveillance for hepatocellular carcinoma with liver ultrasound examination, with or without alpha fetoprotein (AFP), every 6 months is recommended for patients with cirrhosis ^a in accordance with the AASLD guidance on the diagnosis, staging, and management of hepatocellular carcinoma . | Low, Conditional ^b |
| For patients with cirrhosis, endoscopic surveillance for varices should be performed in accordance with the AASLD guidance on portal hypertension bleeding in cirrhosis . | Guidance ^b |
| ^a For decompensated cirrhosis , please refer to the appropriate section. ^b Unlike the AASLD/IDSA HCV guidance, the AASLD guidelines use the GRADE system to rate recommendations; please see that document for further information about this rating system. | |

The Following Monitoring Is Not Recommended During or After Therapy

| NOT RECOMMENDED | RATING  |
|--|--|
| Monitoring for HCV drug resistance-associated substitutions (RASs) during or after therapy is not recommended unless retreatment will be performed. RAS testing is recommended in advance of retreatment therapy. See the Retreatment section for recommendations regarding RAS testing prior to retreatment. Additional information about RAS testing can be found in the HCV Resistance Primer . | IIb, C |

Posttreatment Follow-Up for Patients Who Achieved a Sustained Virologic Response

Recommended Follow-Up for Patients Who Achieved a Sustained Virologic Response (SVR)

| RECOMMENDED | RATING  |
|---|--|
| For noncirrhotic patients, recommended follow-up is the same as if they were never infected with HCV. | I, B |
| Assessment for HCV recurrence is recommended only if the patient develops unexplained hepatic dysfunction, or annual assessment if the patient has ongoing risk factors for HCV infection. In such cases, a quantitative HCV-RNA test rather than an HCV-antibody test is recommended to assess for HCV recurrence. | I, A |


Recommended Follow-Up for Patients Who Achieved a Sustained Virologic Response (SVR)

| | |
|--|-------------------------------|
| Surveillance for hepatocellular carcinoma is recommended for patients with cirrhosis, ^a in accordance with the AASLD guidance on the diagnosis, staging, and management of hepatocellular carcinoma . | Strong, Moderate ^b |
| For cirrhotic patients, upper endoscopic surveillance is recommended in accordance with the AASLD guidance on portal hypertension bleeding in cirrhosis . | Guidance ^b |
| Assessment for other causes of liver disease is recommended for patients who develop persistently abnormal liver tests after achieving SVR. | I, C |

^a For [decompensated cirrhosis](#), please refer to the appropriate section.


^b Unlike the AASLD/IDSA HCV guidance, the AASLD guidelines use the GRADE system to rate recommendations; please [see that document](#) for further information about this rating system.

Monitoring for HCV Infection During Chemotherapy and Immunosuppression


| NOT RECOMMENDED | RATING  |
|--|--|
| Prospective monitoring for HCV recurrence among patients who achieved SVR and are receiving immunosuppressive drug therapy (eg, systemic corticosteroids, antimetabolites, chemotherapy, biologics agents, etc) is not routinely recommended. | III, C |

Additional Considerations If Treatment Includes Ribavirin

Recommended Monitoring During Antiviral Therapy That Includes Ribavirin

| RECOMMENDED | RATING  |
|---|--|
| More frequent assessment for drug-related adverse events (ie, CBC for patients receiving ribavirin) is recommended as clinically indicated. | I, C |

Recommended Monitoring for Pregnancy-Related Issues Prior to and During Antiviral Therapy That Includes Ribavirin

| RECOMMENDED | RATING  |
|--|--|
| Women of childbearing potential and their partners should not receive ribavirin during or for at least 6 months prior to pregnancy. | I, C |
| Women of childbearing potential should be counseled not to become pregnant while receiving a ribavirin-containing antiviral regimen, and for at least 6 months after stopping the regimen. | I, C |
| | |

Recommended Monitoring for Pregnancy-Related Issues Prior to and During Antiviral Therapy That Includes Ribavirin

| | |
|--|------|
| Male partners of women of childbearing potential should be cautioned to prevent pregnancy while they are receiving a ribavirin-containing antiviral regimen, and for up to 6 months after stopping the regimen. | I, C |
| Serum pregnancy testing is recommended for women of childbearing potential prior to beginning treatment with a regimen that includes ribavirin. | I, C |
| Assessment of contraceptive use and of possible pregnancy is recommended at appropriate intervals during (and for 6 months after) ribavirin treatment for women of childbearing potential, and for female partners of men who receive ribavirin treatment. | I, C |

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HCV Resistance Primer

Resistance Testing in Clinical Practice


| Regimen-Specific Recommendations for Use of RAS Testing in Clinical Practice | |
|---|--|
| RECOMMENDED | RATING  |
| Elbasvir/grazoprevir NS5A RAS testing is recommended for genotype 1a-infected, treatment-naïve or -experienced patients being considered for elbasvir/grazoprevir. If present, a different regimen should be considered. | I, A |
| Ledipasvir/sofosbuvir NS5A RAS testing can be considered for genotype 1a-infected, treatment-experienced patients with and without cirrhosis being considered for ledipasvir/sofosbuvir. If clinically important ^a resistance is present, a different recommended therapy should be used. | I, A |
| Sofosbuvir/velpatasvir NS5A RAS testing is recommended for genotype 3-infected, treatment-naïve patients with cirrhosis and treatment-experienced patients (without cirrhosis) being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin should be added or another recommended regimen should be used. | I, A |
| ^a Clinically important = ≥ 100 -fold shift in the in vitro EC ₅₀ to ledipasvir | |

Table 1. Most Common, Clinically Important RASs by DAA, Genotype, and Fold Change

| DAA | Genotype 1a | | | | Genotype 1b | | Genotype 3a | |
|--------------|-------------|-------|---------------|-------------------|---------------|------------|-------------|-------|
| | M28T | Q30R | L31M/V | Y93H/N | L31V/I | Y93H/N | A30K | Y93H |
| Ledipasvir | 20x | >100x | >100x / >100x | >1000x / >10,000x | >100x >50x | >100x / -- | NA | NA |
| Elbasvir | 20x | >100x | >10x >100x | >1000x / >1000x | <10x | >100x / -- | 50x | >100x |
| Velpatasvir | <10x | <3x | 20x / 50x | >100x / >1000x | <3x | <3x / -- | 50x | >100x |
| Pibrentasvir | <3x | <3x | <3x | <10x | <3x | <3x | <3x | <3x |

Color Key: light green = <3-fold change; dark green = <10-fold change; orange = >10- to 100-fold change; pink = >100-fold change

Table 2. Clinically Important RASs by DAA Regimen and Genotype

| DAA Regimen | Genotype | | |
|--------------------------|--|---------------|------|
| | 1a | 1b | 3 |
| Ledipasvir/sofosbuvir | Q30H/R L31M/V Y93C/H/N | L31V ?Y93H | NA |
| Elbasvir/grazoprevir | M28A/T Q30H/R L31M/V Y93C/H/N | Y93H | NA |
| Sofosbuvir/velpatasvir | NA | NA | Y93H |
| Glecaprevir/pibrentasvir | NA | NA | A30K |

Table 3. NS5A RAS Testing Recommendations Prior to Initiation of DAA Treatment Among Genotype 1 Patients by DAA Regimen, Virus Subtype, Prior Treatment Status, and Cirrhosis Status

| DAA Regimen | 1b TN ^a or TE ^b | 1a TN | 1a TE No Cirrhosis | 1a TE Cirrhosis | 3 TN Cirrhosis | 3 TE No Cirrhosis |
|-----------------------|--|----------|--------------------------|-----------------------|----------------------|-------------------------|
| Ledipasvir/sofosbuvir | No | No | Yes | Yes | N/A | N/A |
| Elbasvir/grazoprevir | No | Yes | Yes | Yes | N/A | N/A |

| DAA Regimen | 1b TN ^a or TE ^b | 1a TN | 1a TE No Cirrhosis | 1a TE Cirrhosis | 3 TN Cirrhosis | 3 TE No Cirrhosis |
|--|--|----------|--------------------------|-----------------------|----------------------|-------------------------|
| previr | | | | | | |
| Sofosbuvir/vel patasvir | No | No | No | No | Yes | Yes |
| Glecaprevir/pi brentasvir | No | No | No | No | No | No |
| ^a TN = treatment naive ^b TE = treatment experienced | | | | | | |

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