




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).	IIa, 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) .	IIa, C
<p>Risk Activities</p> <ul style="list-style-type: none"> • Injection drug use (current or ever, including those who injected only once) • Intranasal illicit drug use • Men who have sex with men <p>Risk Exposures</p> <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> ◦ 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 <p>Other Conditions and Circumstances</p> <ul style="list-style-type: none"> • HIV 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
Evaluation for advanced 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

Recommendations for Counseling Persons With Active HCV Infection

Vaccination against pneumococcal infection is recommended for all patients with cirrhosis.	Ila, 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.	Ila, C


Last update: August 27, 2020

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

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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 
<p>Staging of hepatic fibrosis is essential prior to HCV treatment (see Testing and Linkage to Care and see When and in Whom to Treat).</p> <p>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 an online resource such as University of Liverpool interaction checker.)</p>	I, C

Recommended Assessments Prior to Starting DAA Therapy

Patients should be educated about the proper administration of medications (eg, dose, frequency of medicines, food effect, missed doses, adverse effects, 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, albumin, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
- Calculated glomerular filtration rate (eGFR)

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

- Quantitative HCV RNA (HCV viral load)
- If a non-pan-genotypic 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 initiating DAA therapy should be assessed for HIV coinfection.

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 approach to rate recommendations; please see that [document](#) for further information about this rating system.

Recommended Monitoring During Antiviral Therapy

RECOMMENDED


RATING 

Recommended Monitoring During Antiviral Therapy


Clinic visits or telephone contact are recommended as clinically indicated during treatment to ensure medication adherence, and to 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 post-treatment monitoring for hypoglycemia is recommended.	I, C
Inform patients taking warfarin of the potential for changes in their anticoagulation status. On-treatment and post-treatment 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 SVR (cure).	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

Post-Treatment 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.	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
<p>^a For decompensated cirrhosis, please refer to the appropriate section.</p> <p>^b Unlike the AASLD/IDSA HCV guidance, the AASLD guidelines for treatment of chronic hepatitis B uses the GRADE approach to rate recommendations; please see that document for further information about this rating system.</p>	

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 and RAS testing is recommended in advance of this 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

Post-Treatment 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 for treatment of chronic hepatitis B uses the GRADE approach to rate recommendations; please [see that document](#) for further information about this rating system.

Monitoring for HCV 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 effects (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
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	I, C

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


regimen.	
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 
<p>Elbasvir/grazoprevir NS5A RAS testing is recommended for genotype 1a-infected, treatment-naive or -experienced patients being considered for elbasvir/grazoprevir. If present, a different regimen should be considered.</p>	I, A
<p>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.</p>	I, A
<p>Sofosbuvir/velpatasvir NS5A RAS testing is recommended for genotype 3-infected, treatment-naive 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.</p>	I, A

^a Clinically important = ≥ 100 -fold shift in the in vitro EC₅₀ 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

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
Ledipasvir/sofosbuvir	No	No	Yes	Yes
Elbasvir/grazoprevir	No	Yes	Yes	Yes
Sofosbuvir/velpatasvir	No	No	No	No

^a TN = treatment naive
^b TE = treatment experienced

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