

# Making a Decision on When to Initiate HCV Therapy

This is a PDF version of the following document:

Module 4: [Evaluation and Preparation for Hepatitis C Treatment](#)

Lesson 2: [Making a Decision on When to Initiate HCV Therapy](#)

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<https://www.hepatitisC.uw.edu/go/evaluation-treatment/treatment-initiation-decision/core-concept/all>.

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## Indications for Treatment

### Background

Multiple studies have shown that successful antiviral therapy of chronic hepatitis C virus (HCV) infection dramatically reduces both liver-related morbidity (including rates of end-stage liver disease and hepatocellular carcinoma) and mortality, as well as all-cause mortality.[1,2,3,4] Direct-acting antiviral (DAA) treatment for HCV has proven to be much safer, better tolerated, and more effective than treatments used in the interferon era, now rendering the decision to initiate therapy much easier. The AASLD-IDSA HCV Guidance notes that evidence clearly supports treatment of nearly all persons with chronic HCV infection.[5] Decisions regarding initiating therapy will naturally be influenced by the individual's willingness and readiness to undertake treatment.

### Generally Accepted Indicators for Treatment

The AASLD-IDSA HCV Guidance previously provided a priority ranking for treatment based on clinical factors and public health considerations.[5] This priority ranking arose, in part, due to the relatively limited infrastructure capable of treating the surge of persons with chronic HCV infection who had been waiting to receive treatment with new DAA therapy.[5] This treatment priority ranking is no longer used in the AASLD-IDSA HCV Guidance; instead, the current guidance emphasizes that all persons, except for those with a short (i.e. less than 12 months) life expectancy, should receive treatment for chronic HCV infection.[5] The recommendation to treat virtually all persons with chronic HCV infection stems from multiple factors, including the very high sustained virologic response (SVR) rates with current DAA therapy, the safety and tolerability of DAA therapy, and the preponderance of data demonstrating benefit across a spectrum of clinical outcomes with achievement of SVR.[5,6] The AASLD-IDSA HCV Guidance also addresses the following unique populations that may require special considerations when weighing treatment decisions:[5]

- Persons with HCV and HIV coinfection
- Persons with HCV who have decompensated cirrhosis
- Persons who develop HCV post-liver transplantation
- Persons with HCV and renal impairment
- Persons with HCV who are post-renal transplantation
- Persons with acute HCV infection
- Pregnant women with HCV
- Children with HCV

## Contraindications for Treatment

### Absolute Contraindications

In the DAA era, there are relatively few absolute contraindications to HCV treatment with DAAs. The AASLD-IDSA HCV Guidance recommends against treating persons with a short life expectancy that cannot be improved by HCV treatment, liver transplantation, or another directed therapy.[\[5\]](#) Available data from animal studies indicate that ribavirin has significant teratogenic and embryocidal adverse effects.[\[7\]](#) Accordingly, the use of ribavirin is contraindicated in women who are pregnant, women who may become pregnant, or men whose female partners are pregnant or trying to conceive.[\[8,9\]](#) Persons with chronic HCV who are of reproductive age and are to receive a regimen that includes ribavirin should be advised to use two forms of contraception during treatment and for at least 6 months following the end of treatment.[\[10\]](#) With DAA therapy, decompensated cirrhosis, renal failure, and recent or active substance use (e.g. drugs and alcohol) are not contraindications to treatment.[\[11,12,13\]](#) Indeed, multiple studies involving persons with past or current injection-drug use have shown very good adherence and excellent SVR rates with HCV DAA therapy.[\[14,15,16,17\]](#)

### Relative Contraindications

In addition to some absolute contraindications, there are several situations in which the clinician should exert careful consideration before starting HCV treatment: active severe substance use disorder that would interfere with making follow-up appointments; psychiatric issues that are not well controlled; and social issues that may negatively impact an individual's ability to adhere with therapy, to make visits for monitoring treatment safety, or to show up for scheduled office visits.[\[18,19\]](#) Since there are no large-scale studies on the use of pangenotypic DAA regimens during pregnancy, the AASLD-IDSA HCV Guidance recommends initiation of HCV therapy before trying to conceive.[\[5\]](#) For children with HCV, DAA therapy should be deferred until at least 3 years of age, as there are no approved DAA regimens for children younger than 3 years of age.[\[5\]](#) Ledipasvir-sofosbuvir is approved for the treatment of HCV genotypes 1, 4, 5, or 6 starting at 3 years of age, with the pangenotypic regimens sofosbuvir-velpatasvir and glecaprevir-pibrentasvir approved starting at ages 6 and 12 years, respectively.[\[5\]](#)

## Treatment Readiness

### Assessing Readiness

An individual's readiness to start therapy can be difficult to assess, but a checklist can be used as a general guide ([Figure 1](#)). It is important to have a frank discussion with each person considering HCV treatment about the chance of cure, the potential side effects of therapy, the cost of treatment, and, if using a regimen that includes ribavirin, the impact of treatment on their quality of life, including deferring pregnancy.

### Pretreatment Counseling

In addition, the HCV pretreatment discussion should cover counseling on adherence, drug interactions, potential side effects, contact numbers for after-hour questions or issues, and specific information on follow-up visits. Given the high cost of DAAs and the potential for drug resistance, it is very important that persons considering HCV treatment understand fully the importance of remaining 100% adherent with the treatment regimen.

## Timing of Initiation of Treatment

The availability of DAAs has provided tremendous opportunities for highly effective, convenient, well-tolerated therapy. Although the high cost of these medications remains a concern, the cost of DAA therapy has significantly decreased over the past several years, and many states are now covering DAA therapy for all Medicaid and Medicare patients without restriction. Nevertheless, some state Medicaid plans continue to have fibrosis, sobriety, and prescriber restrictions for DAA therapy.[\[20\]](#) These restrictions are not in step with AASLD-IDSA HCV Guidance and represent a suboptimal and short-sighted approach to care.[\[5,21,22,23\]](#) If possible, DAA therapy should be initiated in all persons with chronic HCV and not deferred due to ongoing substance use or fibrosis requirements.

## Advanced Age and Comorbid Conditions

Many persons living with chronic HCV infection in the United States are over 50 years of age. With the availability of new, highly effective, safe, well-tolerated regimens, it is likely that more interest and experience will accumulate in treating persons with advanced age. Notably, some clinical trials with newer direct-acting antivirals have enrolled persons older than 70 years of age, but overall relatively little experience exists with treatment of HCV in elderly populations. In some circumstances, individuals with chronic HCV may have advanced age and minimal HCV-related fibrosis, and thus HCV-related liver disease may not be expected to play a major role in shortening their lifespan. In addition, some individuals may have limited life expectancy due to other comorbid conditions, and as such, HCV treatment would not be expected to alter their quality of life or life expectancy. Thus, in some situations involving persons with advanced age or significant medical comorbidities associated with an expected short lifespan (less than 12 months), it may be sensible to withhold therapy.

## Obtaining Authorization and Payment for Medications

If an individual with chronic HCV has been deemed an appropriate candidate for antiviral therapy, the medical provider should begin investigating payment for the HCV treatment. Because these antiviral agents are quite costly, they typically need to be preapproved. The authorization process may take several weeks, with the exact time dependent on the insurance coverage and state of residence. Restrictions vary by state and insurer as to who can prescribe DAAs, as well as the level of fibrosis and sobriety. In addition, individuals with HCV waiting to start treatment should be warned in advance that the DAA medication approval process may be drawn out.

## Monitoring and Follow-Up if Not Treated

### General Recommendations for Monitoring and Follow-Up

There may be various reasons for deferring HCV treatment, including specific barriers that are present for the individual considering treatment, such as active psychosocial instability, a competing severe illness, or insurance denial. At least annual follow-up is recommended for these individuals. During these follow-up visits, counseling should occur regarding behaviors that will optimize liver health, including avoiding a diet high in saturated fat, achieving an optimal body weight, limiting intake of hepatotoxic medications, and abstaining from or limiting alcohol intake. Medical providers should be aware of indicators associated with accelerated hepatic fibrosis progression, such as older age at the time of HCV infection, male sex, alcohol consumption, nonalcoholic steatohepatitis (NASH), genotype 3 HCV, and coinfection with HIV and/or hepatitis B virus (HBV) ([Figure 2](#)).[\[24,25,26\]](#) Individuals who have indicators associated with accelerated hepatic fibrosis should receive counseling regarding the risk and impact of accelerated hepatic fibrosis progression; in this setting, clinicians should attempt to promptly initiate HCV treatment. These individuals also should receive information and education on the warning signs and symptoms of liver dysfunction, including jaundice, melena, clay-colored stools, confusion, abdominal distention, and lower extremity edema.[\[27,28\]](#) Finally, persons with chronic HCV should receive counseling on the HCV transmission and strategies on how to prevent transmission of HCV to others.

### Reassessing Hepatic Fibrosis

For individuals with chronic HCV and mild to moderate fibrosis (F0 to F2), progression of liver fibrosis can occur. As such, they should undergo annual monitoring with laboratory studies that include aspartate aminotransferase (AST), alanine aminotransferase (ALT), complete blood cell count (CBC), and platelet count. From these basic laboratory tests, an AST to Platelet Ratio Index (APRI) and/or a FIB-4 index can be calculated.[\[29,30\]](#) In addition, subsequent noninvasive testing to reevaluate hepatic fibrosis, such as FibroSure, FibroTest, ActiTest, or transient elastography, is recommended.[\[31,32\]](#) The optimal interval for reevaluating hepatic fibrosis may depend on clinical factors and the stage of liver disease. For individuals with cirrhosis, hepatocellular carcinoma (HCC) surveillance with a liver ultrasound, with or without alpha-fetoprotein (AFP), is recommended every 6 months.[\[33,34\]](#)

### Monitoring and Assistance with an Unstable Psychosocial Situation

Individuals living with chronic HCV who have an unstable psychosocial situation should have these issues addressed by referring to appropriate resources, such as a mental health professional or a substance use disorder counselor. Ongoing alcohol use disorder is a high priority to address since it can markedly accelerate hepatic fibrosis; for this reason, persons with chronic HCV should receive a clear and strong counseling message to completely abstain from alcohol intake.[\[31,35\]](#) Special effort should be made to address psychosocial issues in persons with advanced fibrosis (F3 or F4), since they have a more immediate need for HCV treatment.

## Summary Points

- The availability of highly effective, convenient, safe, well-tolerated therapy has changed the landscape for HCV treatment.
- Nearly all persons with chronic HCV will benefit from therapy; persons with a severely limited lifespan (less than 12 months) are the exception.
- For nearly all persons with chronic HCV, DAAs should be initiated and not deferred due to ongoing substance use or fibrosis requirements.
- In situations when HCV treatment is deferred (for whatever reason), the individual should periodically undergo reevaluation for disease progression and reconsideration of treatment, with the frequency of reevaluation individualized based on the person's current fibrosis stage, likely fibrosis progression rate, and other factors that may influence treatment readiness.

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## Figures

**Figure 1 Suggested Checklist Prior to Initiating Treatment for Chronic HCV**

<b>Checklist Before Starting Hepatitis C Therapy</b>
<b>General Checklist for All Patients</b>
<input type="checkbox"/> Willing to adhere with DAA therapy and follow-up visits
<input type="checkbox"/> Psychiatrically stable
<input type="checkbox"/> Drug and/or alcohol use evaluated and addressed so as not to interfere with therapy
<input type="checkbox"/> Potential drug interactions addressed and plan in place to monitor
<b>IF Treatment with Ribavirin</b>
<input type="checkbox"/> Not pregnant or planning to become pregnant during therapy and for 6 months afterwards
<input type="checkbox"/> If patient or partner of child-bearing potential, willing to use $\geq 2$ reliable birth control methods
<input type="checkbox"/> No significant cardiac or respiratory issues

**Figure 2 Factors Associated with Accelerated Hepatic Fibrosis**

Source: American Association for the Study of Liver Disease, the Infectious Diseases Society of America. When and in whom to initiate HCV therapy. Recommendations for testing, management, and treating hepatitis C.

AASLD/IDSA: HCV Guidance	
Factors Associated with Accelerated Fibrosis Progression	
Host	Viral
<ul style="list-style-type: none"> <li>▪ <b>Non Modifiable</b></li> <li>Fibrosis stage</li> <li>Inflammation grade</li> <li>Older age at time of infection</li> <li>Male sex</li> <li>Organ transplant</li> </ul>	<ul style="list-style-type: none"> <li>Genotype 3</li> <li>Coinfection with HBV or HIV</li> </ul>
<ul style="list-style-type: none"> <li>▪ <b>Modifiable</b></li> <li>Alcohol consumption</li> <li>Nonalcoholic fatty liver disease</li> <li>Obesity</li> <li>Insulin resistance</li> </ul>	