

# HCV Simplified Treatment

This is a PDF version of the following document:

Module 8: [HCV Test and Cure](#)

Lesson 4: [HCV Simplified Treatment](#)

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<https://www.hepatitisC.uw.edu/go/test-cure/hcv-simplified-treatment/core-concept/all>.

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## Eligibility for Simplified HCV Treatment

### Who is Eligible for HCV Treatment?

The American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD-IDSA) Hepatitis C Guidance recommends treatment for ALL persons with chronic hepatitis C virus (HCV) infection, except for individuals who have a short (e.g., less than 12 months) life expectancy.[1] The landscape of hepatitis C care has been revolutionized by the discovery and widespread use of direct-acting antivirals (DAAs) to treat HCV infection. The DAAs are safe, highly effective, well-tolerated, and provide a cure to more than 95% of persons who receive an 8- or 12-week course with one of the currently recommended pangenotypic regimens. Treatment of HCV with DAAs has been shown to reduce the risk of hepatic complications such as hepatocellular carcinoma and liver-related mortality.[1] Further, HCV treatment with cure has the public health benefit of preventing transmission of HCV. Decisions regarding initiation of therapy will naturally be influenced by the individual's willingness and readiness to start. It is important that HCV therapy not be withheld based on active substance use, older age, or mental health illness, as none of these are a contraindication to treatment.[Q] Eligibility for HCV Treatment

### Who is Eligible for Simplified HCV Treatment?

The AASLD-IDSA HCV Guidance has devised a simplified HCV treatment approach, which can be used most HCV treatment-naïve adult patients.[2,3] This simplified approach has been made possible with the availability of the safe, highly effective, pangenotypic DAA regimens glecaprevir-pibrentasvir and sofosbuvir-velpatasvir. The following summarizes the AASLD-IDSA HCV Guidance regarding eligibility for the simplified HCV treatment approach.[2,4,5]

This simplified HCV approach is appropriate for adults with chronic HCV, including persons with HIV, who meet the following criteria:

- **Any HCV Genotype:** Persons with any HCV genotype are eligible for the simplified treatment approach. This approach is made possible because the recommended regimens in the simplified treatment (glecaprevir-pibrentasvir and sofosbuvir-velpatasvir) have pangenotypic activity.
- **Treatment-Naïve:** Only persons who are HCV treatment-naïve adults are considered appropriate for the simplified approach. Patients are not eligible for this simplified approach if they have previously received HCV treatment since prior treatment may be associated with development of drug resistance and may necessitate adjustments to therapy.
- **Without Cirrhosis or with Compensated Cirrhosis:** The simplified treatment approach is considered appropriate for persons without cirrhosis and for those with compensated cirrhosis (Child-

Turcotte-Pugh A). For this context, cirrhosis should have been evaluated as outlined in the prior lesson.

## Who is NOT Eligible for Simplified HCV Treatment?

Although most adult patients are eligible for the simplified treatment approach, the AASLD-IDSA HCV Guidance recommends against using the simplified treatment in certain situations. The following summarizes specific conditions that, if present, should preclude use of the simplified treatment approach.[\[2,5\]](#)

- **Prior HCV Treatment:** Prior DAA exposure may result in the development of resistance-associated substitutions (RAS). Because of this, alternative regimens for HCV treatment may be needed in these populations.[\[6,7\]](#)
- **Hepatitis B Surface Antigen-Positive:** Reactivation of HBV has been increasingly recognized as a potential adverse event associated with treatment of HCV.[\[8,9,10\]](#) The risk of reactivation is highest among hepatitis B surface antigen (HBsAg)-positive patients, but rare cases have been described in HBsAg-negative and hepatitis B core antibody (anti-HBc) positive patients.[\[11,12\]](#) Patients who are HBsAg positive may need initiation of HBV antiviral therapy concurrently with initiation of HCV treatment versus close monitoring while on DAAs.[\[13\]](#) Patients who are HBsAg-negative but anti-HBc-positive can be monitored with alanine aminotransferase (ALT) levels at baseline, at the end of HCV treatment, and at post-treatment follow-up.[\[13\]](#)
- **Compensated Cirrhosis with End-Stage Renal Disease:** Individuals with cirrhosis that is compensated (Child-Turcotte-Pugh score

## Recommended Regimens for Simplified Treatment

There are two equally recommended DAA options to use for the simplified treatment of persons with chronic HCV: (1) an 8-week treatment course with oral glecaprevir-pibrentasvir and (2) a 12-week treatment course with oral sofosbuvir-velpatasvir.[2,3,5] Both of these regimens have pangenotypic activity, have once-daily dosing, are well-tolerated, and have cure rates greater than 95% with all HCV genotypes. The following table and text provide additional details about these two medications and the recommendations for use in the simplified treatment for adults without cirrhosis or adults with compensated cirrhosis. Table 2.

### Medications Used in Simplified HCV Treatment

Med	Glecaprevir-Pibrentasvir	Sofosbuvir-Velpatasvir
Trade Name	<i>Mavyret</i>	<i>Epclusa</i>
Adult dose (oral)	Glecaprevir 300 mg and pibrentasvir 120 mg once daily, taken as 3 tablets once daily	Sofosbuvir 400 mg and velpatasvir 100 mg single tablet once daily
Duration*	8 weeks	12 weeks <sup>#</sup>
Food requirement	Take with food.	Take with or without food.
Hepatic impairment	Contraindicated in patients with decompensated liver disease (Child-Turcotte-Pugh B or C).	No dose adjustment necessary (Child-Turcotte-Pugh A, B, or C).
Renal impairment	No dosage adjustment is recommended in patients with any degree of renal impairment, including patients with end-stage renal disease on dialysis.	No dosage adjustment is recommended in patients with any degree of renal impairment, including patients on dialysis.
Notable drug interactions <i>See Prescribing Information for full list and details of drug interactions</i>	<p>Coadministration with <b>ethinyl estradiol</b> or any ethinyl estradiol-containing medications is contraindicated. Glecaprevir-pibrentasvir can increase levels of hormone and cause ALT elevation.</p> <p>Coadministration is contraindicated with <b>rifampin</b> due to potential loss of therapeutic effect with glecaprevir-pibrentasvir.</p> <p>Coadministration is not recommended with certain HMG-CoA Reductase Inhibitors (<b>atorvastatin, lovastatin, or simvastatin</b>); use with other HMG-CoA Reductase Inhibitors may require dose adjustment of the HMG-CoA Reductase Inhibitor.</p> <p>Coadministration is not recommended with <b>carbamazepine</b> due to the potential loss of therapeutic effect with glecaprevir-pibrentasvir.</p> <p>Coadministration is not recommended with some <b>HIV antiretroviral medications</b>, including HIV protease inhibitors and some non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz and etravirine).<sup>^</sup></p> <p>Coadministration is not recommended with <b>St. John's Wort</b> (hypericum perforatum) due to the potential loss of therapeutic effect with glecaprevir-pibrentasvir.</p> <p>Coadministration is not recommended with <b>cyclosporin</b> when the dose of cyclosporin is &gt;100 mg daily.</p>	<p>Coadministration with <b>proton pump inhibitors</b> is recommended. If medically necessary, should be taken with food or antacids once daily. Use of other PPIs and antacids has not been studied.</p> <p>Coadministration is not recommended with <b>rifapentine</b> due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with medication <b>amiodarone</b> due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with <b>carbamazepine, phenytoin, or valproic acid</b> due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with medication <b>efavirenz</b>.</p> <p>Coadministration is not recommended with <b>St. John's Wort</b> (hypericum perforatum) due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with medication <b>topotecan</b>.</p>

Med	Glecaprevir-Pibrentasvir	Sofosbuvir-Velpatasvir
	mg/day.	
<p>*In treatment-naïve individuals without cirrhosis or with compensated cirrhosis. Treatment for patients with decompensated cirrhosis is discussed in this discussion.</p> <p>#Note: patients with compensated cirrhosis and HCV genotype 3 should have treatment guided by HCV genotypic drug-resistance testing. If drug-resistance testing does not show the NS5A resistance associated substitutions (RAS) Y93H, then the 12-week sofosbuvir-velpatasvir regimen is recommended. If resistance testing shows NS5A RAS Y93H, then weight-based ribavirin should be added to the 12-week sofosbuvir-velpatasvir regimen. The recommended regimen should be chosen (e.g., glecaprevir-pibrentasvir one daily for 8 weeks or sofosbuvir-velpatasvir one daily for 12 weeks).</p> <p>**See <a href="#">Liverpool HCV drug interaction site</a></p> <p>^See AASLD/IDSA guidance section on HIV and HCV coinfection.</p>		

[Q] GP Drug Interactions

## Glecaprevir-Pibrentasvir

Glecaprevir-pibrentasvir is the first pangenotypic NS3/4A protease inhibitor-NS5A inhibitor combination to be approved that offers a potent treatment option for most patients with chronic HCV, including an 8-week option for HCV treatment-naïve patients.

- **Efficacy:** In the main registration trials, sustained virologic response (SVR) rates for 8 or 12 weeks of glecaprevir-pibrentasvir for HCV genotypes 1-6 were greater than 95% with very few on-treatment virologic breakthroughs or posttreatment relapses.[21,22]
- **Adult Dosing and Duration:** The recommended dosing is three tablets taken once daily with food for 8 weeks.
- **Contraindications:** This drug is not an option for patients with decompensated cirrhosis (Child-Turcotte-Pugh B or C), given the presence of the protease inhibitor.
- **Notable Drug Interactions:** Statin therapy may need to be held or dose adjusted during treatment with glecaprevir-pibrentasvir. Coadministration with ethinyl estradiol is contraindicated since glecaprevir-pibrentasvir can increase estrogen hormone levels and cause ALT elevation. Potential drug interactions can occur with some HIV antiretroviral medications, including HIV protease inhibitors and the non-nucleoside reverse transcriptase inhibitors efavirenz and etravirine.
- **Dosing with Renal Impairment:** No dosage adjustment is recommended in patients with any degree of renal impairment, including patients with end-stage renal disease who are receiving dialysis.
- **Dosing with Hepatic Impairment:** Use of glecaprevir-pibrentasvir is contraindicated in patients with decompensated liver disease (Child-Turcotte-Pugh B or C).

## Sofosbuvir-Velpatasvir

Sofosbuvir-velpatasvir is a pangenotypic NS5A-NS5B inhibitor single-pill combination regimen that has potent activity against HCV genotypes 1-6.

- **Efficacy:** In the main registration trials, SVR rates for 12 weeks for HCV genotypes 1-6 were in the range of 95-100% with very few virologic breakthroughs or posttreatment relapses.[20,23,24]
- **Adult Dosing and Duration for Persons without Cirrhosis:** The recommended dosing is one tablet taken once daily with or without food for 12 weeks.
- **Adult Dosing and Duration for Persons with Compensated Cirrhosis:** Patients with compensated cirrhosis who will be treated with sofosbuvir-velpatasvir should have an HCV genotype performed. Individuals with HCV genotype 1, 2, 4, 5, or 6 should be treated with the same regimen as used for persons without cirrhosis (one tablet taken once daily with or without food for 12 weeks). Persons with HCV genotype 3 should have further evaluation with HCV genotypic drug-resistance testing, with treatment guided by these results. If drug-resistance testing does not show the NS5A resistance-associated substitution (RAS) Y93H, then the same sofosbuvir-velpatasvir regimen listed above can be used (one tablet taken once daily with or without food for 12 weeks). If resistance testing shows NS5A RAS Y93H, then weight-based ribavirin should be added to the 12-week sofosbuvir-velpatasvir regimen.

regimen, or another recommended regimen should be chosen (e.g., glecaprevir-pibrentasvir once daily for 8 weeks).

- **Contraindications:** Sofosbuvir-velpatasvir can, in contrast to HCV protease-inhibitor-containing regimens, be used safely in persons with decompensated cirrhosis.
- **Notable Drug Interactions:** Levels of velpatasvir can be significantly reduced with concurrent use of acid-reducing agents, particularly proton-pump inhibitors. If a proton-pump inhibitor is medically indicated, then the manufacturer advises that sofosbuvir-velpatasvir be taken with food 4 hours before dosing omeprazole 20 mg daily. Other proton-pump inhibitors and other doses have not been adequately studied to recommend coadministration.
- **Renal Impairment:** No dosage adjustment is recommended in patients with any degree of renal impairment, including patients with end-stage renal disease on dialysis.
- **Dosing with Hepatic Impairment:** No dose adjustment is necessary with sofosbuvir-velpatasvir for any degree of hepatic impairment (Child-Turcotte-Pugh A, B, or C).

[Activity] C. Recommended Regimens for Simplified Treatment Approach

# Monitoring and Management Related to HCV Treatment

## Laboratory Monitoring During HCV Treatment

The following summarizes recommendations for laboratory monitoring in the AASLD-IDSA HCV Guidance [2,3] during HCV treatment of individuals using the simplified treatment approach.

### Laboratory Monitoring Recommendations

- For all persons receiving the simplified treatment approach, routine HCV RNA monitoring during treatment is not recommended.[2,3]
- In patients without cirrhosis, routine laboratory monitoring is not required during HCV treatment with DAA therapy, unless they have one of the special indications listed below (diabetes or receiving anticoagulation).[3]
- In patients with compensated cirrhosis, a hepatic function panel can be sent at 4 and 8 weeks after starting treatment, with the rationale that liver decompensation can rarely occur among persons with cirrhosis who are receiving HCV treatment. Since the risk of major hepatotoxicity with these agents is very low, this is not a strong recommendation.[2] If an individual has worsening of liver blood tests, such as a significant increase in bilirubin, ALT, or aspartate aminotransferase (AST), they should be referred to a specialist.[2]
- Hepatic function panel assessment during and at the end of treatment is reasonable to consider among those individuals whom you suspect have metabolic dysfunction-associated steatotic liver disease (MASLD) as a contributing factor to liver enzyme elevation. Patients who do not have complete normalization of their ALT/AST on therapy may require further follow-up or evaluation.

### Special Considerations in Persons with Diabetes

- Observational data have shown that chronic HCV infection can impair glycemic control.[25] Direct-acting antiviral (DAA) therapy and HCV clearance have been shown to improve glycemic control in patients with diabetes, as evidenced by a decrease in mean hemoglobin A1c and decreased insulin use.[25,26]
- Patients taking medications to treat diabetes, particularly insulin and sulfonylureas, should be counseled about the potential increased risk of developing hypoglycemia while receiving DAA treatment and after successful DAA treatment.[27] Symptoms and warning signs for hypoglycemia should be reviewed. Providers should note that insulin and other diabetes medication dose adjustments may be indicated during and following HCV treatment.[Q] Impact of HCV Treatment on Diabetes

### Special Considerations in Persons Receiving Anticoagulation

- Fluctuations in INR values may occur in patients receiving warfarin concurrent with HCV treatment. This has been described as reduced warfarin sensitivity in most cases.[28] The mechanism is unclear but may reflect cytochrome P450 interactions as well as improvement in hepatic function and vitamin K metabolism.
- Clinicians should be aware of this potential drug interaction and plan to monitor INR closely during HCV treatment and minimize subtherapeutic levels of anticoagulation.[2,3]
- Drug interactions have not been observed with coadministration of HCV treatment with direct oral anticoagulants (DOACs).[29]

## Laboratory Testing after Completing HCV Treatment

The following summarizes recommendations for laboratory monitoring at the end of the simplified HCV treatment (or soon thereafter).[2,3]

## Test-of-Cure: Sustained Virologic Response

It is recommended to check a quantitative HCV RNA level as a test-of-cure following HCV treatment. This is preferentially done 12 weeks (or more) following completion of treatment. Given high rates of patients lost to follow-up at 12 weeks post treatment, an alternative option is to obtain an HCV RNA 4 weeks post treatment in patients without cirrhosis or prior DAA exposure.[2,3] At either 12 weeks or 4 weeks post treatment, the goal is to achieve an undetectable HCV RNA, known as a sustained virologic response (SVR). Although achieving an SVR at 12 weeks (SVR12) is the gold standard for HCV cure, randomized controlled trials have shown greater than 99% concordance between SVR12 and SVR4 in patients without cirrhosis and without prior DAA exposure.[30,31] Although the SVR12 and SVR4 rates typically exceed 95%, achieving an SVR cannot be assumed after treatment completion and must be confirmed.[2,3] An SVR is considered a durable virologic cure, with multiple studies demonstrating that more than 99% of patients who achieve SVR continue to have undetectable HCV RNA in the blood years after therapy, unless they acquire HCV again.[32,33] In addition, achieving an SVR has also been shown to result in long-term clinical benefits with improved event-free survival.[34,35][Activity] E. Follow up After the HCV Test and Treat Approach

## Checking Hepatic Function Panel

Checking a hepatic function panel at least 12 weeks after completing treatment is also recommended, especially for individuals who have significant baseline elevations in ALT and/or AST levels.[2,3] Liver fibrosis, as well as liver aminotransferase levels, can improve after SVR. Therefore, individuals who achieve an SVR and do not have cirrhosis or other factors that would contribute to chronic liver disease (e.g., excessive alcohol use or metabolic dysfunction-associated steatotic liver disease) do not require further HCV or liver-related clinical monitoring.

## Management of Incomplete DAA Adherence

Incomplete adherence to DAAs is relatively common among persons receiving treatment for HCV and has the potential to impact SVR12 rates.[36,37] Although short periods of nonadherence are unlikely to affect response to treatment, longer periods of nonadherence can lead to virologic failure.[38,39] Based on published literature and expert consensus, the AASLD-IDSA HCV Guidance has issued recommendations for the management of nonadherence events that factor in the duration of nonadherence and whether the nonadherence event(s) occurred within or after the first 28 days of therapy (Table 3).[5] It is important to note that these recommendations are intended to address nonadherence events in treatment-naïve individuals who qualify for the simplified treatment algorithm and are receiving glecaprevir-pibrentasvir or sofosbuvir-velpatasvir. Management of incomplete adherence in patients who fall outside this guidance should be done in consultation with an HCV specialist. It is also important to note that in these recommendations, the phrase “restart DAA therapy immediately” means restarting the current treatment course and does not mean restarting from day 1 of treatment. Because treatment interruptions longer than 7 days require further investigation and increase the likelihood of virologic failure, patients should be instructed to notify their provider if they miss more than 7 days of therapy at any point in their DAA treatment course.

## Supplemental Case Study Exercises

The following interactive case studies are intended to provide a quick assessment and review of HCV simplified treatment, with questions related to criteria, regimen choices, indications for genotypic, monitoring response to treatment, and management of treatment interruptions.

[Activity] D. Initiation of HCV Treatment in Person with Alcohol Use Disorder

[Activity] E. Glecaprevir-Pibrentasvir Treatment with Compensated Cirrhosis

[Activity] F. What is the next step that should be taken for this patient?

[Activity] G. Drug Interactions with Glecaprevir-Pibrentasvir

[Activity] H. Drug Interactions with Sofosbuvir-Velpatasvir

[Activity] I. Management of Treatment Interruption with less than 7 Missed Days

[Activity] J. Management of Treatment Interruption After Missing 8-20 Days



## Summary Points

All persons with chronic HCV infection should be treated except individuals who have a less than 12-month life expectancy; treating HCV in persons who inject drugs is a high priority to eliminate the impact of the HCV epidemic in the United States and globally.

The discovery and widespread use of pangenotypic DAAs to treat HCV has led to the AASLD-IDSA recommendation for a simplified HCV treatment approach, expanding the health care workforce able to provide HCV treatment. The AASLD-IDSA simplified HCV treatment algorithm provides specific criteria for the inclusion and exclusion of treatment-naïve persons.

There are two recommended simplified treatment courses for persons with chronic HCV: oral glecaprevir-pibrentasvir and oral sofosbuvir-velpatasvir; both have pangenotypic activity, once-daily dosing, cure rates greater than 95%, and are well-tolerated.

The glecaprevir-pibrentasvir 8-week treatment regimen consists of 3 tablets taken once daily with food; it is not an option for persons with decompensated cirrhosis.

The sofosbuvir-velpatasvir 12-week regimen consists of 1 tablet taken once daily with or without food with no dose adjustment necessary for hepatic impairment; persons with compensated cirrhosis should have a genotype performed as persons with HCV genotype 3 may require an alternative regimen or the addition of weight-based ribavirin.

Routine laboratory monitoring during simplified treatment with DAAs is not needed for most patients, but posttreatment monitoring should include a test-of-cure to determine whether they achieved an SVR.

Individuals with incomplete medication adherence during treatment should be managed based on how far into treatment they are and how many days of medication doses are missed.

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## Figures

**Figure 1 Simplified Treatment Criteria**

Based on the AASLD/IDSA eligibility criteria for the simplified treat approach for treating HCV,  
select the correct eligibility button for each group listed below.

1 of 12

Age greater than 60 years

ELIGIBLE for Simplified Treatment

NOT ELIGIBLE for Simplified Treatment

Correct: 0

Incorrect: 0

Show All Correct Answers

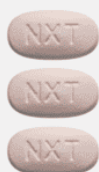
Start Over



**Figure 2 Simplified Treatment Medication Options**

## AASLD-IDSA Simplified HCV Treatment Patients WITHOUT Cirrhosis

### Glecaprevir-Pibrentasvir (Mavyret)



8 weeks

3 pills once daily (with food) x 8 weeks

### Sofosbuvir-Velpatasvir (Epclusa)



12 weeks

1 pill once daily (+/- food) x 12 weeks

**Figure 3 HCV Treatment Exercises**

## HCV Simplified Treatment: Case Study Exercises

< 1 2 3 4 5 6 7 >

START

< Previous Question Skip Question > ✓ Check Answer

Table 1. **AASLD/IDSA HCV Guidance: Simplified HCV Treatment Eligibility Criteria**

Who is Eligible for Simplified HCV Treatment Algorithm	Who is Not Eligible for Simplified HCV Treatment Algorithm
<p><b>Adults with chronic HCV infection who are treatment-naïve, including:</b></p> <ul style="list-style-type: none"> <li>Any HCV genotype</li> <li>HIV coinfection</li> <li>Persons without cirrhosis <u>or</u> with compensated cirrhosis (Child-Turcotte-Pugh A*)</li> </ul>	<p><b>Adults with chronic HCV infection who are not eligible for simplified treatment:</b></p> <ul style="list-style-type: none"> <li>Previously received HCV treatment</li> <li>Hepatitis B surface antigen (HBsAg) positive</li> <li>Decompensated cirrhosis (Child-Turcotte-Pugh B or C)</li> <li>Current or prior decompensation (ascites, encephalopathy, or variceal hemorrhage)</li> <li>Current pregnancy</li> <li>Known or suspected hepatocellular carcinoma</li> <li>Prior liver transplantation</li> </ul>

Source:

- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naïve Adults With Compensated Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)]
- AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naïve Adults Without Cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)]

Table 2.

### Medications Used in Simplified HCV Treatment

Med	Glecaprevir-Pibrentasvir	Sofosbuvir-Velpatasvir
Trade Name	<i>Mavyret</i>	<i>Epclusa</i>
Adult dose (oral)	Glecaprevir 300 mg and pibrentasvir 120 mg once daily, taken as 3 tablets once daily	Sofosbuvir 400 mg and velpatasvir 100 mg single tablet once daily
Duration*	8 weeks	12 weeks <sup>#</sup>
Food requirement	Take with food.	Take with or without food.
Hepatic impairment	Contraindicated in patients with decompensated liver disease (Child-Turcotte-Pugh B or C).	No dose adjustment necessary (Child-Turcotte-Pugh A, B, or C).
Renal impairment	No dosage adjustment is recommended in patients with any degree of renal impairment, including patients with end-stage renal disease on dialysis.	No dosage adjustment is recommended in patients with any degree of renal impairment, including patients on dialysis.
Notable drug interactions <i>See Prescribing Information for full list and details of drug interactions</i>	<p>Coadministration with <b>ethinyl estradiol</b> or any ethinyl estradiol-containing medications is contraindicated. Glecaprevir-pibrentasvir can increase levels of hormone and cause ALT elevation.</p> <p>Coadministration is contraindicated with <b>rifampin</b> due to potential loss of therapeutic effect with glecaprevir-pibrentasvir.</p> <p>Coadministration is not recommended with certain HMG-CoA Reductase Inhibitors (<b>atorvastatin, lovastatin, or simvastatin</b>); use with other HMG-CoA Reductase Inhibitors may require dose adjustment of the HMG-CoA Reductase Inhibitor.</p> <p>Coadministration is not recommended with <b>carbamazepine</b> due to the potential loss of therapeutic effect with glecaprevir-pibrentasvir.</p> <p>Coadministration is not recommended with some <b>HIV antiretroviral medications</b>, including HIV protease inhibitors and some non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz and etravirine).<sup>^</sup></p> <p>Coadministration is not recommended with <b>St. John's Wort</b> (hypericum perforatum) due to the potential loss of therapeutic effect with glecaprevir-pibrentasvir.</p> <p>Coadministration is not recommended with <b>cyclosporin</b> when the dose of cyclosporin is &gt;100 mg/day.</p>	<p>Coadministration with <b>proton pump inhibitors</b> is recommended. If medically necessary, should be taken with food once daily. Use of other PPIs and H<sub>2</sub> antagonists has not been studied.</p> <p>Coadministration is not recommended with <b>rifapentine</b> due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with medication <b>amiodarone</b> due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with <b>carbamazepine, phenytoin</b> due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with medication <b>efavirenz</b>.</p> <p>Coadministration is not recommended with <b>St. John's Wort</b> (hypericum perforatum) due to potential loss of therapeutic effect with sofosbuvir-velpatasvir.</p> <p>Coadministration is not recommended with medication <b>topotecan</b>.</p>

\*In treatment-naïve individuals without cirrhosis or with compensated cirrhosis. Treatment for patients with decompensated cirrhosis is discussed in this discussion.

<sup>#</sup>Note: patients with compensated cirrhosis and HCV genotype 3 should have treatment guided by HCV genotypic and resistance testing. If resistance testing does not show the NS5A resistance associated substitutions (RAS) Y93H, then the 12-week sofosbuvir-velpatasvir regimen is recommended. If resistance testing shows NS5A RAS Y93H, then weight-based ribavirin should be added to the 12-week sofosbuvir-velpatasvir recommended regimen should be chosen (e.g., glecaprevir-pibrentasvir one daily for 8 weeks or sofosbuvir-velpatasvir plus weight-based ribavirin for 12 weeks).

\*\*See [Liverpool HCV drug interaction site](#)

Med	Glecaprevir-Pibrentasvir	Sofosbuvir-Velpatasvir
^ See AASLD/IDSA guidance section on HIV and HCV coinfection.		

**Table 3. AASLD/IDSA HCV Guidance: Simplified HCV Treatment for Treatment-Naïve Adults Without Cirrhosis**

**Recommended Management of DAA Treatment Interruptions for Treatment-Naïve Patients without Cirrhosis or with Compensated Cirrhosis Receiving Glecaprevir-Pibrentasvir or Sofosbuvir-Velpatasvir**

<b>Interruptions <u>Before</u> Receiving 28 Days of DAA Therapy</b>	
<b>Missed <math>\leq 7</math> Days</b>	<ul style="list-style-type: none"> <li>• <b>Restart</b> DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).</li> </ul>
<b>Missed <math>\geq 8</math> Days</b>	<ul style="list-style-type: none"> <li>• <b>Restart</b> DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.</li> <li>• <b>Obtain</b> HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy. <ul style="list-style-type: none"> <li>◦ If HCV RNA is negative (undetectable), complete originally planned DAA treatment course (8 or 12 weeks; total planned dosage<sup>a</sup>). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 infection and/or compensated cirrhosis.</li> <li>◦ If HCV RNA is positive (<math>&gt;25</math> IU/L) or not obtained, extend DAA treatment for an additional 4 weeks.</li> </ul> </li> </ul>
<b>Interruptions <u>After</u> Receiving <math>\geq 28</math> Days of DAA Therapy</b>	
<b>Missed <math>\leq 7</math> Days</b>	<ul style="list-style-type: none"> <li>• <b>Restart</b> DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).</li> </ul>
<b>Missed 8-20 Consecutive Days</b>	<ul style="list-style-type: none"> <li>• <b>Restart</b> DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.</li> <li>• <b>Obtain</b> HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy. <ul style="list-style-type: none"> <li>◦ If HCV RNA is negative (undetectable), complete originally planned DAA treatment course (8 or 12 weeks; total planned dosage<sup>a</sup>). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 infection and/or compensated cirrhosis.</li> <li>◦ If HCV RNA is positive (<math>&gt;25</math> IU/L) or not obtained, <b>stop</b> DAA treatment and retreat according to recommendations in the Retreatment Section in the AASLD-IDSA Guidance.</li> </ul> </li> </ul>
<b>Missed <math>\geq 21</math> Consecutive Days</b>	<ul style="list-style-type: none"> <li>• <b>Stop</b> DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to recommendations in the Retreatment Section.</li> </ul>
Abbreviations: DAA = direct-acting antiviral; HCV = hepatitis C virus; SVR = sustained virologic response <sup>a</sup> Extend duration of therapy such that the patient receives the total planned dosage (ie, the total number of daily pills). For example, if a patient missed 10 days of a planned 8-week course of therapy, treatment would be extended to 8 weeks plus 10 days.	

Source:

- Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clin Infect Dis. 2023 May 25;ciad319. [[PubMed Abstract](#)]

