

Treatment of HCV Genotype 2

This is a PDF version of the following document:

Section 5: [Treatment of Chronic Hepatitis C Infection](#)

Topic 2: [Treatment of HCV Genotype 2](#)

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<https://www.hepatitisc.uw.edu/go/treatment-infection/treatment-genotype-2/core-concept/all>.

Introduction

Background

In the United States, genotype 2 accounts for approximately 13 to 15% of all hepatitis C infections.[1] In the era before direct-acting antiviral agents (DAAs), sustained virologic response rates at 12 weeks post-treatment (SVR12) were relatively higher in persons with genotype 2 than those with genotype 1, 3, or 4; genotype 2 infection has been considered the most readily treatable genotype. Thus, data regarding retreatment of individuals with genotype 2 in whom prior therapy failed is somewhat limited. The following discussion regarding initial treatment and retreatment of patients with genotype 2 chronic hepatitis C assumes the patient and their clinician have already made the decision to proceed with hepatitis C therapy.

Medications Used to Treat HCV Genotype 2

The [HCV Medications](#) section on this web site provides detailed information for each of the FDA-approved medications listed in the treatment recommendations, including links to the full prescribing information and to patient assistance programs. The direct-acting antiviral agents exert their action at specific steps in the HCV life cycle. There are three major classes of direct-acting antiviral medications: nonstructural proteins 3/4A (NS3/4A) protease inhibitors, NS5A inhibitors, and NS5B polymerase inhibitors ([Figure 1](#)); the NS5B polymerase inhibitors include the nucleoside analogs and nonnucleoside analogs.[2,3] Adherence with the treatment regimen is of paramount importance. Accordingly, patients should receive detailed counseling regarding the importance of adherence prior to starting therapy and clinicians should provide intensive follow-up during therapy.

Approach to Choosing HCV Genotype 2 Treatment Regimen

For patients chronically infected with genotype 2 HCV, two key factors influence the choice and duration of therapy: cirrhosis status and prior treatment experience. In addition, the cost of the regimen, insurance coverage, and patient and provider preference can play a major role in the regimen choice. For initial treatment of patients with genotype 2 HCV infection, the estimated wholesale acquisition cost for regimens in the recommended category in the American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD-IDSA) HCV Guidance ranges from approximately \$26,400 to \$74,760 for those without cirrhosis and from \$39,600 to \$74,760 for those with compensated cirrhosis ([Figure 2](#)). The following treatment recommendations are based on the AASLD-IDSA HCV Guidance for patients with genotype 2 HCV.[4,5]

- [AASLD-IDSA HCV Guidance for Treatment-Naïve Patients with Genotype 2 HCV](#)
- [AASLD-IDSA HCV Guidance for Treatment-Experienced Patients with Genotype 2 HCV](#)

HCV Genotype 2: Initial Treatment

Background

Historically, in the interferon era, treatment of genotype 2 infection achieved higher sustained virologic response (SVR) rates than with genotype 1 infection, even with a shorter duration of therapy and lower doses of ribavirin. Prior to the availability of direct-acting antiviral agents, the standard of care for treatment-naïve patients with genotype 2 hepatitis C consisted of a 24-week course of peginterferon plus fixed-dose ribavirin, with SVR rates of 75 to 85%.[\[6,7,8,9\]](#) In 2013, the combination of sofosbuvir with peginterferon and ribavirin showed greater than 90% SVR12 rates in genotype 2 infection.[\[10\]](#) Later that year, the United States Food and Drug Administration (FDA) approved a 12-week course with the all-oral regimen of sofosbuvir plus ribavirin for the treatment of genotype 2 infection based on data from several studies showing SVR rates of approximately 92 to 97% with this regimen.[\[11,12,13\]](#) In 2015, daclatasvir plus sofosbuvir was FDA approved as the first interferon- and ribavirin-free combination for genotype 2 infection and this 12-week combination produced SVR rates of greater than 95%.[\[14,15\]](#) Most recently, SVR rates of 99% have been reported with sofosbuvir-velpatasvir or glecaprevir-pibrentasvir for initial treatment of patients with genotype 2 HCV.[\[16,17,18,19\]](#)

Factors to Consider Prior to Choosing Initial Treatment Regimen

For initial treatment of patients chronically infected with genotype 2 hepatitis C two major factors influence the choice of regimen and duration of therapy: (1) the presence or absence of cirrhosis, and (2) cost or insurance considerations. The treatment regimens and duration of therapy for patients with HCV-HIV coinfection are the same as for those for HCV mono-infection. Hepatitis C therapy in patients with decompensated cirrhosis, renal impairment, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD-IDSA HCV Guidance for Initial Treatment of HCV Genotype 2

The following is a summary of the AASLD-IDSA HCV Guidance for initial treatment of patients with chronic hepatitis C genotype 2 infection.[\[20,21\]](#) For individuals with cirrhosis, the AASLD-IDSA HCV Guidance defines compensated cirrhosis as Child-Turcotte-Pugh class A and decompensated cirrhosis as Child-Turcotte-Pugh class B or class C. The recommended regimens are listed by evidence level; when the evidence level is considered equivalent, the regimens are listed alphabetically.

Table 1. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Alternative for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

<p>Daclatasvir *(60 mg) one tablet once daily for 12 weeks</p>	+	<p>Sofosbuvir (400 mg) one tablet once daily for 12 weeks</p>
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Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 2 without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 2. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir
Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir
**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

Rating: [Class I](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Alternative for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

<p>Daclatasvir *(60 mg) one tablet once daily for 16-24 weeks</p>	+	<p>Sofosbuvir (400 mg) one tablet once daily for 16-24 weeks</p>
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Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

^For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 2 with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Key Studies for Initial Treatment of Patients with Genotype 2

The following key studies support the recommendations for treatment-naïve patients with chronic hepatitis C and genotype 2 infection.

Daclatasvir plus Sofosbuvir

- [AI444040](#): In study AI444040, a phase 2 trial involving adults with genotypes 1, 2, and 3, all participants received daclatasvir plus sofosbuvir, with or without ribavirin. A total of 44 treatment-naïve adults with genotype 2 or 3 were enrolled in the study, including 26 with genotype 2 infection.[[14](#)] The participants with genotype 2 or 3 received one of three 24-week regimens: (1) daclatasvir plus sofosbuvir, with the first week consisting of sofosbuvir alone, (2) daclatasvir plus sofosbuvir, and (3) daclatasvir plus sofosbuvir plus ribavirin. Among the treatment-naïve adults with genotype 2 infection, 92% (24 of 26) achieved an SVR12. For the 2 individuals with genotype 2 who were classified as not having an SVR12, one was lost to follow-up (but had an undetectable HCV RNA at treatment week 14) and the other did not return for all of the post-treatment visits (but had an undetectable HCV RNA level at post-treatment week 24). All regimens were well-tolerated and safe.
- [ALLY-2](#): This phase 3 trial enrolled treatment-naïve and treatment-experienced adults with chronic HCV genotype 1-4 and HIV coinfection.[[15](#)] The treatment-naïve participants received an 8-week or 12-week course of daclatasvir plus sofosbuvir. For the 17 treatment-naïve genotype 2 participants, the SVR12 rates were 100% (11 of 11) in those who received 12-weeks of therapy and 83% (5 of 6) with the 8-week course of therapy.

Glecaprevir-Pibrentasvir

- [EXPEDITION-1](#): This phase 3 single-arm open-label trial evaluated the safety and efficacy of a 12-week course of glecaprevir-pibrentasvir in treatment-naïve and treatment-experienced adults with compensated cirrhosis and HCV genotype 1, 2, 4, 5, or 6 infection.[[16](#)] A total of 31 participants with genotype 2 infection received treatment and 100% (31 of 31) achieved an SVR12.
- [ENDURANCE-2](#): This phase 3 randomized, double-blind placebo-controlled trial evaluated the safety and efficacy of 12 weeks of therapy with glecaprevir-pibrentasvir in adults with genotype 2 hepatitis C infection without cirrhosis.[[17](#)] Among those enrolled, 70% percent were treatment-naïve. Overall, when excluding 6 sofosbuvir-experienced participants, 99% (195 of 196) achieved an SVR12 by intent-to-treat analysis. There were no serious adverse events related to glecaprevir-pibrentasvir.

Sofosbuvir-Velpatasvir

- [ASTRAL-2](#): The ASTRAL-2 trial was a randomized, open-label phase 3 study that compared the safety and efficacy of the fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks with sofosbuvir plus ribavirin for 12 weeks in treatment-naïve and treatment-experienced adults with chronic HCV genotype 2 infection.[[19](#)] Patients with compensated cirrhosis

comprised 14% of the total 266 patients enrolled in the study. In the treatment-naïve participants who received sofosbuvir-velpatasvir, 99% (114 of 115) achieved an SVR12 compared with 95% (106 of 111) in those who received sofosbuvir plus ribavirin. The one individual who did not achieve an SVR12 in the sofosbuvir-velpatasvir group had received only one dose of the drug and discontinued after experiencing headache and anxiety. For treatment-naïve participants in the sofosbuvir-velpatasvir group, there was no difference in SVR12 rates between those without cirrhosis and those with compensated cirrhosis (99% versus 100%).

HCV Genotype 2: Retreating Persons who Failed Prior Therapy

Background

Prior to the introduction of direct-acting antiviral agents, the SVR rates with treatment of genotype 2 infection was approximately 75 to 85%. Accordingly, less clinical experience exists with retreatment of patients with genotype 2 than with genotype 1 infection. In particular, very limited data exist with retreatment of genotype 2 patients with cirrhosis. Recent trial data suggest either of the pangenotypic combinations of sofosbuvir-velpatasvir or glecaprevir-pibrentasvir are highly effective in treatment-experienced patients with HCV genotype 2 infection.[\[16,17,18,19\]](#)

Factors to Consider Prior to Choosing Retreatment Regimen

For retreatment of patients with genotype 2 hepatitis C, three major factors influence the optimal regimen for retreatment, including (1) the prior regimen the patient failed, (2) presence or absence of cirrhosis, and (3) cost or insurance considerations. The retreatment of genotype 2 patients with decompensated cirrhosis, renal impairment, HIV coinfection, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD-IDSA HCV Guidance for Retreatment of HCV Genotype 2

The following is a summary of the AASLD-IDSA HCV Guidance for patients with hepatitis C genotype 2 infection in whom (1) prior peginterferon and ribavirin therapy failed, or (2) prior sofosbuvir plus ribavirin therapy failed.[\[22,23,24\]](#) For individuals with cirrhosis, the AASLD-IDSA HCV Guidance defines compensated cirrhosis as Child-Turcotte-Pugh class A and decompensated cirrhosis as Child-Turcotte-Pugh class B or class C. The recommended regimens are listed by evidence level; when the evidence level is considered equivalent, the regimens are listed alphabetically.

Table 3. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

<p>Daclatasvir <i>*(60 mg) one tablet once daily for 12 weeks</i></p>	+	<p>Sofosbuvir <i>(400 mg) one tablet once daily for 12 weeks</i></p>
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Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 patients without cirrhosis [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 4. AASLD-IDSA HCV Guidance for Genotype 2 Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir
Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir
**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

Rating: [Class I](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

<p>Daclatasvir <i>*(60 mg) one tablet once daily for 16-24</i></p>	+	<p>Sofosbuvir <i>(400 mg) one tablet once daily for 16-24</i></p>
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weeks

weeks

Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

^For treatment of patients with decompensated cirrhosis, see the AASLD-IDSa Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSa. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 with compensated cirrhosis. [[AASLD-IDSa Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 5. AASLD-IDSa HCV Guidance for Genotype 2: Retreatment Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^

Recommended regimens listed by evidence level.

Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level B](#)

Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis^

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

Rating: [Class IIb](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

^For treatment of patients with decompensated cirrhosis, see the AASLD-IDSa Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSa. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: sofosbuvir plus ribavirin-experienced, genotype 2 patients with or without compensated cirrhosis. [[AASLD-IDSa Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Key Studies for Retreatment of Adults with HCV Genotype 2

The following key studies support the recommendations for retreatment of patients with chronic hepatitis C and genotype 2 infection who previously failed therapy.

Glecaprevir-Pibrentasvir

- [ENDURANCE-2](#): This phase 3 randomized, double-blind placebo-controlled trial evaluated the safety and efficacy of 12 weeks of therapy with glecaprevir-pibrentasvir in adults with genotype 2 hepatitis C infection without cirrhosis.[17] Thirty percent were treatment-experienced; most (91%) had received interferon-based while the remainder had previous sofosbuvir-based therapy. Among DAA-naïve participants who received glecaprevir-pibrentasvir, 99% (195 of 196) achieved a sustained virologic response 12 (SVR12) by intent-to-treat analysis. None of the 61 treatment-experienced participants had virologic failure. There were no serious adverse events related to glecaprevir-pibrentasvir.
- [SURVEYOR-II \(Part 4\)](#): This phase 3, single-arm, open-label trial evaluated the safety and efficacy of 8 weeks of glecaprevir-pibrentasvir in 203 adults with genotype 2, 4, 5 or 6 infection without cirrhosis.[17] Among those enrolled, 71% (145 of 203) had genotype 2 infection and 12% of the patients with genotype 2 were treatment-experienced. For all participants with genotype 2 infection, 98% (142 of 145) had a sustained virologic response rate (SVR12).

Sofosbuvir-Velpatasvir

- [ASTRAL-2](#): The ASTRAL-2 was a randomized, open-label phase 3 trial that compared the safety and efficacy of sofosbuvir-velpatasvir versus sofosbuvir plus ribavirin, both for 12 weeks in treatment-naïve and treatment-experienced adults with chronic HCV genotype 2 infection.[17] Participants with compensated cirrhosis were permitted and comprised 14% of the total 266 persons enrolled in the study. Overall, the SVR12 rate among sofosbuvir-velpatasvir recipients was 99% (133 of 134) and was superior to the SVR12 rate of 94% (124 of 132) among those who received sofosbuvir plus ribavirin. For the treatment-experienced participants treated with sofosbuvir-velpatasvir, 100% (19 of 19) achieved an SVR12, including 15 without cirrhosis and 4 with compensated cirrhosis.
- [POLARIS-2](#): The POLARIS-2 trial was a phase 3, open-label trial, for treatment-naïve and treatment-experienced adults with chronic hepatitis C genotype 1-4 infection who were randomized to either 8 weeks of sofosbuvir-velpatasvir-voxilaprevir or 12 weeks of sofosbuvir-velpatasvir.[25] Prior treatment with peginterferon and ribavirin was allowed, but not prior treatment with direct-acting antiviral therapy. Compensated cirrhosis was present in 18% of participants. For the genotype 2 recipients of 12 weeks of sofosbuvir-velpatasvir, 100% (53 of 53) achieved an SVR12; the SVR12 was 97% (61 of 63) among those who received 8 weeks of sofosbuvir-velpatasvir-voxilaprevir.
- [POLARIS-4](#): In this phase 3, active-comparator, open-labeled trial, 314 adults with chronic hepatitis C genotype 1-3 and prior direct-acting antiviral (DAA) therapy without an NS5A inhibitor were randomized to receive a 12-week treatment course with either sofosbuvir-velpatasvir-voxilaprevir or sofosbuvir-velpatasvir.[26] Compensated cirrhosis was present in 46% and prior sofosbuvir exposure in 80% of participants. For those with genotype 2 HCV, 97% (32 of 33) treated with sofosbuvir-velpatasvir achieved an SVR12 and 100% (31 of 31) achieved an SVR12 with sofosbuvir-velpatasvir-voxilaprevir.

HCV Genotype 2: Treatment Regimen under Study

A new combination currently being investigated for genotype 2 infection is described below. This regimen is not yet approved for use and not currently recommended as standard therapy.

- **Grazoprevir-Ruzasvir-Uprifosbuvir (MK-3682)**. This 3-class DAA combination that includes grazoprevir (NS3/4 protease inhibitor) coformulated with ruzasvir, a novel NS5A inhibitor and uprifosbuvir, a novel NS5B inhibitor is currently being studied, with or without ribavirin, in the C-CREST trials in treatment-naïve patients with genotype 2 infection. The 12-week option without ribavirin was shown to be highly effective (97%) in phase 2 trials in genotype 2 infected patients. [[27](#),[28](#),[29](#)]

Summary Points

- The recommended regimens for initial treatment of HCV genotype 2 in patients without cirrhosis are glecaprevir-pibrentasvir for 8 weeks or sofosbuvir-velpatasvir for 12 weeks; the alternative is daclatasvir plus sofosbuvir for 12 weeks.
- For initial treatment of genotype 2 patients with compensated cirrhosis, the recommended regimens are either glecaprevir-pibrentasvir or sofosbuvir-velpatasvir for 12 weeks; the alternative, daclatasvir plus sofosbuvir, should be given for 16 to 24 weeks.
- For the retreatment of genotype 2 patients previously treated with peginterferon plus ribavirin, with or without compensated cirrhosis, the recommended and alternative regimens are the same as for initial therapy of genotype 2.
- For retreatment of genotype 2 patients who previously failed therapy with sofosbuvir plus ribavirin, the recommended regimens are (1) glecaprevir-pibrentasvir for 12 weeks or (2) sofosbuvir-velpatasvir for 12 weeks; the same regimens are used in patients with or without compensated cirrhosis.

Citations

1. Germer JJ, Mandrekar JN, Bendel JL, Mitchell PS, Yao JD. Hepatitis C virus genotypes in clinical specimens tested at a national reference testing laboratory in the United States. *J Clin Microbiol.* 2011;49:3040-3.
[\[PubMed Abstract\]](#) -
2. Manns MP, Buti M, Gane E, et al. Hepatitis C virus infection. *Nat Rev Dis Primers.* 2017;3:17006.
[\[PubMed Abstract\]](#) -
3. Scheel TK, Rice CM. Understanding the hepatitis C virus life cycle paves the way for highly effective therapies. *Nat Med.* 2013;19:837-49.
[\[PubMed Abstract\]](#) -
4. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Treatment-Naive Genotype 2.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
5. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Treatment-Experienced Genotype 2.
[\[AASLD-IDSA Hepatitis C Guidance\]](#) -
6. Dalgard O, Bjørø K, Ring-Larsen H, et al. Pegylated interferon alfa and ribavirin for 14 versus 24 weeks in patients with hepatitis C virus genotype 2 or 3 and rapid virological response. *Hepatology.* 2008;47:35-42.
[\[PubMed Abstract\]](#) -
7. Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med.* 2002;347:975-82.
[\[PubMed Abstract\]](#) -
8. Hadziyannis SJ, Sette H Jr, Morgan TR, et al. Peginterferon-alfa2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. *Ann Intern Med.* 2004;140:346-55.
[\[PubMed Abstract\]](#) -
9. Zeuzem S, Hultcrantz R, Bourliere M, et al. Peginterferon alfa-2b plus ribavirin for treatment of chronic hepatitis C in previously untreated patients infected with HCV genotypes 2 or 3. *J Hepatol* 2004;40:993-9.
[\[PubMed Abstract\]](#) -
10. Lawitz E, Lalezari JP, Hassanein T, et al. Sofosbuvir in combination with peginterferon alfa-2a and ribavirin for non-cirrhotic, treatment-naive patients with genotypes 1, 2, and 3 hepatitis C infection: a randomised, double-blind, phase 2 trial. *Lancet Infect Dis.* 2013;13:401-8.
[\[PubMed Abstract\]](#) -
11. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. *N Engl J Med.* 2013;368:1878-87.
[\[PubMed Abstract\]](#) -
12. Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. *N Engl J Med.* 2013;368:1867-77.
[\[PubMed Abstract\]](#) -

13. Zeuzem S, Dusheiko GM, Salupere R, et al. Sofosbuvir and ribavirin in HCV genotypes 2 and 3. *N Engl J Med.* 2014;370:1993-2001.
[\[PubMed Abstract\]](#) -
14. Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. *N Engl J Med.* 2014;370:211-21.
[\[PubMed Abstract\]](#) -
15. Wyles DL, Ruane PJ, Sulkowski MS, et al. Daclatasvir plus sofosbuvir for HCV in patients coinfecting with HIV-1. *N Engl J Med.* 2015;373:714-25.
[\[PubMed Abstract\]](#) -
16. Forns X, Lee SS, Valdes J, et al. Glecaprevir plus pibrentasvir for chronic hepatitis C virus genotype 1, 2, 4, 5, or 6 infection in adults with compensated cirrhosis (EXPEDITION-1): a single-arm, open-label, multicentre phase 3 trial. *Lancet Infect Dis.* 2017;17:1062-1068.
[\[PubMed Abstract\]](#) -
17. Asselah T, Kowdley KV, Zadeikis N, et al. Efficacy of Glecaprevir/Pibrentasvir for 8 or 12 Weeks in Patients With Hepatitis C Virus Genotype 2, 4, 5, or 6 Infection Without Cirrhosis. *Clin Gastroenterol Hepatol.* 2018;16:417-426.
[\[PubMed Abstract\]](#) -
18. Feld JJ, Jacobson IM, Hézode C, et al. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *N Engl J Med.* 2015;373:2599-607.
[\[PubMed Abstract\]](#) -
19. Foster GR, Afdhal N, Roberts SK, et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med.* 2015;373:2608-17.
[\[PubMed Abstract\]](#) -
20. AASLD-IDS. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 2 with compensated cirrhosis.
[\[AASLD-IDS Hepatitis C Guidance\]](#) -
21. AASLD-IDS. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 2 without cirrhosis.
[\[AASLD-IDS Hepatitis C Guidance\]](#) -
22. AASLD-IDS. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: sofosbuvir plus ribavirin-experienced, genotype 2 patients with or without compensated cirrhosis.
[\[AASLD-IDS Hepatitis C Guidance\]](#) -
23. AASLD-IDS. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 patients without cirrhosis
[\[AASLD-IDS Hepatitis C Guidance\]](#) -
24. AASLD-IDS. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 with compensated cirrhosis.
[\[AASLD-IDS Hepatitis C Guidance\]](#) -
25. Jacobson IM, Lawitz E, Gane EJ, et al. Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials.

Gastroenterology. 2017;153:113-22.

[[PubMed Abstract](#)] -

26. Bourlière M, Gordon SC, Flamm SL, et al. Sofosbuvir, Velpatasvir, and Voxilaprevir for Previously Treated HCV Infection. *N Engl J Med*. 2017;376:2134-46.
[[PubMed Abstract](#)] -
27. Gane EJ, Pianko S, Roberts SK, et al. Safety and efficacy of an 8-week regimen of grazoprevir plus ruzasvir plus uprifosbuvir compared with grazoprevir plus elbasvir plus uprifosbuvir in participants without cirrhosis infected with hepatitis C virus genotypes 1, 2, or 3 (C-CREST-1 and C-CREST-2, part A): two randomised, phase 2, open-label trials. *Lancet Gastroenterol Hepatol*. 2017;2:805-813.
[[PubMed Abstract](#)] -
28. Lawitz E, Buti M, Vierling JM, et al. Safety and efficacy of a fixed-dose combination regimen of grazoprevir, ruzasvir, and uprifosbuvir with or without ribavirin in participants with and without cirrhosis with chronic hepatitis C virus genotype 1, 2, or 3 infection (C-CREST-1 and C-CREST-2, part B): two randomised, phase 2, open-label trials. *Lancet Gastroenterol Hepatol*. 2017;2:814-823.
[[PubMed Abstract](#)] -
29. Wyles D, Wedemeyer H, Ben-Ari Z, et al. Grazoprevir, ruzasvir, and uprifosbuvir for hepatitis C virus after NS5A treatment failure. *Hepatology*. 2017;66:1794-1804.
[[PubMed Abstract](#)] -

References

- Foster GR, Pianko S, Brown A, et al. Efficacy of sofosbuvir plus ribavirin with or without peginterferon-alfa in patients with hepatitis C virus genotype 3 infection and treatment-experienced patients with cirrhosis and hepatitis C virus genotype 2 infection. *Gastroenterology*. 2015;149:1462-70.
[[PubMed Abstract](#)] -
- Hagan LM, Yang Z, Ehteshami M, Schinazi RF. All-oral, interferon-free treatment for chronic hepatitis C: cost-effectiveness analyses. *J Viral Hepat*. 2013;20:847-57.
[[PubMed Abstract](#)] -
- Jacobson IM, Brown RS Jr, Freilich B, et al. Peginterferon alfa-2b and weight-based or flat-dose ribavirin in chronic hepatitis C patients: a randomized trial. *Hepatology*. 2007;46:971-81.
[[PubMed Abstract](#)] -
- Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. *N Engl J Med*. 2013;368:1867-77.
[[PubMed Abstract](#)] -
- Summa V, Ludmerer SW, McCauley JA, et al. MK-5172, a selective inhibitor of hepatitis C virus NS3/4a protease with broad activity across genotypes and resistant variants. *Antimicrob Agents Chemother*. 2012;56:4161-7.
[[PubMed Abstract](#)] -
- Wang C, Jia L, O'Boyle DR 2nd, et al. Comparison of daclatasvir resistance barriers on NS5A from hepatitis C virus genotypes 1 to 6: implications for cross-genotype activity. *Antimicrob Agents Chemother*. 2014;58:5155-63.
[[PubMed Abstract](#)] -

- Zeuzem S, Dusheiko GM, Salupere R, et al. Sofosbuvir and ribavirin in HCV genotypes 2 and 3. N Engl J Med. 2014;370:1993-2001.
[[PubMed Abstract](#)] -

Figures

Figure 1 Classes of Direct-Acting Antiviral Agents Used to Treat HCV

NS3/4A Protease Inhibitors	NS5A Inhibitors	NS5B Polymerase Inhibitors
Boceprevir	Daclatasvir	Dasabuvir
Glecaprevir	Elbasvir	Sofosbuvir
Grazoprevir	Ledipasvir	
Paritaprevir	Ombitasvir	
Simeprevir	Pibrentasvir	
Telaprevir	Velpatasvir	
Voxilaprevir		

Figure 2 Cost of Medication Regimens used to Treat Genotype 2 Chronic HCV

This figure shows the approximate cost of a treatment course with AASLD-IDSA recommended regimens for treatment-naïve patients with genotype 2 chronic HCV, including those without cirrhosis and those with compensated cirrhosis. The cost listed is based on available wholesale acquisition price data.

Estimated Cost of Recommended Regimens for Initial Treatment HCV GT2	
Regimens and Duration of Therapy	Cost of Regimen*
Genotype 2 HCV Without Cirrhosis	
Glecaprevir-Pibrentasvir for 8 weeks	\$26,400
Sofosbuvir-Velpatasvir for 12 weeks	\$74,760
Genotype 2 HCV With Compensated Cirrhosis	
Glecaprevir-Pibrentasvir for 12 weeks	\$39,600
Sofosbuvir-Velpatasvir for 12 weeks	\$74,760
*Cost estimates based on Wholesale Acquisition Cost (WAC)	

Table 1. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Recommended for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Alternative for Treatment-Naïve Genotype 2 Patients Without Cirrhosis

Daclatasvir

**(60 mg) one tablet once daily for 12 weeks*

+

Sofosbuvir

(400 mg) one tablet once daily for 12 weeks

Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 2 without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 2. AASLD-IDSA HCV Guidance for Genotype 2: Initial Treatment Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Recommended for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

Rating: [Class I](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Alternative for Treatment-Naïve Genotype 2 Patients With Compensated Cirrhosis[^]

Daclatasvir

**(60 mg) one tablet once daily for 16-24 weeks*

+

Sofosbuvir

(400 mg) one tablet once daily for 16-24 weeks

Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

[^]For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 2 with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 3. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*

Rating: [Class I](#), [Level A](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Daclatasvir

**(60 mg) one tablet once daily for 12 weeks*

+

Sofosbuvir

(400 mg) one tablet once daily for 12 weeks

Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 patients without cirrhosis [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 4. AASLD-IDSA HCV Guidance for Genotype 2 Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Recommended and alternative regimens listed by evidence level and alphabetically

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level A](#)

Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

Rating: [Class I](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis[^]

Daclatasvir

**(60 mg) one tablet once daily for 16-24 weeks*

+

Sofosbuvir

(400 mg) one tablet once daily for 16-24 weeks

Rating: [Class IIa](#), [Level B](#)

Note: *The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. See the daclatasvir prescribing information for details.

[^]For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 2 with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

Table 5. AASLD-IDSA HCV Guidance for Genotype 2: Retreatment Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis[^]

Recommended regimens listed by evidence level.

Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis[^]

Sofosbuvir-Velpatasvir

Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks

Rating: [Class I](#), [Level B](#)

Recommended for Sofosbuvir plus Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis[^]

Glecaprevir-Pibrentasvir

**Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*

Rating: [Class IIb](#), [Level B](#)

Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).

[^]For treatment of patients with decompensated cirrhosis, see the AASLD-IDSA Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: sofosbuvir plus ribavirin-experienced, genotype 2 patients with or without compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

