

# Treatment of HCV Genotype 1

This is a PDF version of the following document:

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

Topic 1: [Treatment of HCV Genotype 1](#)

You can always find the most up to date version of this document at

<https://www.hepatitisc.uw.edu/go/treatment-infection/treatment-genotype-1/core-concept/all>.

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## Introduction

### Background

In the United States, genotype 1 hepatitis C virus (HCV) accounts for approximately 70 to 75% of all HCV infections.[1] Accordingly, treatment of genotype 1 has the most extensive data and highest clinical relevance for hepatitis C treatment issues in the United States. In recent years, multiple studies using direct-acting antiviral agents have shown sustained virologic response rates at 12 weeks post-treatment (SVR12) of greater than 95% in treatment-naïve and treatment-experienced genotype 1 patients, including those with compensated cirrhosis. The high cost of these very effective regimens has limited the widespread implementation of hepatitis treatment in the United States, but recently, lower priced options have become available. For initial treatment of patients with genotype 1a HCV infection (without cirrhosis), the estimated wholesale acquisition cost for the regimens recommended by 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 \$94,500 (Figure 1); the cost of initial treatment of patients with genotype 1a and compensated cirrhosis ranges from \$39,600 to \$94,500 (Figure 2). The following discussion regarding initial treatment and retreatment of patients with genotype 1 chronic HCV assumes the patient and their clinician have already made the decision to initiate hepatitis C therapy.

### Medications used to Treat HCV Genotype 1

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; the NS5B polymerase inhibitors include the nucleoside analogs and nonnucleoside analogs (Figure 3).[2,3] Adherence with the treatment regimen is of paramount importance. Patients should receive detailed counseling regarding the importance of adherence prior to starting therapy as well as intensive monitoring and follow-up during therapy.

### Approach to Choosing HCV genotype 1 Treatment Regimen

For patients chronically infected with genotype 1 HCV, three key factors influence the choice and duration of therapy: (1) the genotype 1 subtype (1a or 1b), (2) cirrhosis status, and (3) prior treatment experience. With use of certain regimens for patients with genotype 1A infection, the presence of baseline NS5A resistance may also be relevant for all or a subset of these patients. In addition, the cost of the regimen, insurance coverage, and provider preference can play a major role in the regimen choice. The AASLD-IDSA have issued regularly updated guidance on the treatment of patients with hepatitis C. The following treatment recommendations are based on the AASLD-IDSA

HCV Guidance for patients with genotype 1 HCV.[4,5]

- [AASLD-IDS A HCV Guidance for Treatment-Naïve Patients with Genotype 1 HCV](#)
- [AASLD-IDS A HCV Guidance for Treatment-Experienced Patients with Genotype 1 HCV](#)

# HCV Genotype 1: Initial Treatment

## Background

The treatment landscape for treatment-naïve patients with genotype 1 chronic HCV infection has rapidly changed in recent years. Historically, genotype 1 hepatitis C was considered the most difficult to treat hepatitis C genotype. From 1998 to 2013, therapy evolved from interferon monotherapy, to peginterferon monotherapy, to peginterferon plus ribavirin, to triple therapy with peginterferon plus ribavirin plus an NS3A/4A protease inhibitor (boceprevir or telaprevir).[\[6,7,8,9\]](#) In late 2013 and most of 2014, the standard of care for initial therapy of genotype 1 consisted of peginterferon plus ribavirin plus either sofosbuvir or simeprevir.[\[10,11,12,13\]](#) Since 2015, the standard of care for genotype 1 has consisted of all-oral therapy with a combination of direct-acting antiviral agents (DAAs). In 2017, there are multiple safe, convenient, and highly effective all-oral regimens recommended for the treatment of HCV genotype 1, most of which do not require ribavirin.

## Factors to Consider Prior to Choosing Initial Treatment Regimen

For treatment-naïve patients chronically infected with genotype 1 hepatitis C, three key factors influence the choice and duration of therapy: (1) genotype 1 subtype (1a or 1b) and (2) presence or absence of cirrhosis, and (3) cost or insurance considerations. If the genotype 1 subtype is not known, the patient should be treated as genotype 1a. The baseline HCV RNA value generally does not influence the treatment choice or duration, except in treatment-naïve noncirrhotic patients in whom 8 or 12 weeks of ledipasvir-sofosbuvir is being considered. A post-hoc analysis from the ION-3 trial in treatment-naïve patients without cirrhosis noted that participants with a baseline HCV RNA level less than 6 million IU/mL had similar relapse rates using 8 or 12 weeks of therapy.[\[14\]](#) Additional data from the HCV-TARGET registry and the Veterans Affairs National Healthcare System demonstrated comparable high SVR rates of 94 to 98% for patients with either 8 or 12 weeks of ledipasvir-sofosbuvir among noncirrhotic patients with baseline HCV RNA levels less than 6 million IU/mL.[\[15\]](#)

In addition to the factors noted above, drug interactions may also influence the choice of therapy, particularly for patients coinfecting with HIV who are taking antiretroviral medications. Of note, individuals with HCV and HIV coinfection are eligible for most of the same regimens as HCV monoinfected patients, except for the 8-week option of ledipasvir-sofosbuvir. The presence of decompensated cirrhosis, renal impairment, acute hepatitis C infection, or post-liver transplantation can each impact choice of treatment regimens and/or duration of therapy and these special circumstances are addressed in Module 6, [Treatment of Special Populations and Special Situations](#).

## Baseline Resistance Testing

In treatment-naïve patients, baseline resistance testing is not recommended for most of the first-line DAA regimens, with the exception of elbasvir-grazoprevir. Pretreatment NS5A resistance testing is recommended for all patients with HCV genotype 1a in whom elbasvir-grazoprevir is being considered to detect the presence of virus with NS5A resistance-associated substitutions at the amino acid positions 28, 30, 31, or 93, which are associated with inferior treatment response.[\[16\]](#) The presence of one or more of these resistance-associated substitutions (present in up to 10% of naïve patients) requires the addition of ribavirin to the regimen and extending the treatment course of elbasvir-grazoprevir from 12 to 16 weeks.[\[16\]](#) The 16-week combination of elbasvir-grazoprevir plus ribavirin is more complex and considered an alternative regimen. Genotypic resistance testing is commercially available through several laboratories and typically costs less than \$1000.

## AASLD-IDS A HCV Guidance for Initial Treatment of HCV Genotype 1

The following is a summary of the AASLD-IDS A HCV Guidance recommendations for the initial

treatment of patients with hepatitis C genotype 1a or 1b infection; these recommendations include separate tables for patients without cirrhosis and for those with compensated cirrhosis.<sup>[17,18,19,20]</sup> 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 1a: Initial Treatment Treatment-Naïve Genotype 1a Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Treatment-Naïve Genotype 1a Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Recommended for Treatment-Naïve Genotype 1a 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 1a Patients Without Cirrhosis**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

**Recommended for Treatment-Naïve Genotype 1a Patients Without Cirrhosis**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 8 weeks*

For patients who are non-black, HIV-uninfected, and whose HCV RNA level is

# HCV Genotype 1: Retreating Persons who Failed Prior Therapy

## Background

New DAA combinations have markedly improved treatment outcomes for patients with genotype 1 HCV who have failed prior therapy, with SVR12 rates exceeding 95%. Given the very high SRV rates both with initial treatment and retreatment using DAAs, the number of treatment-experienced patients is diminishing as a sub-population. Prior failure with a regimen that included an NS3/4A protease inhibitor (boceprevir or telaprevir) does not impact subsequent therapy with the NS5A inhibitors (ledipasvir or ombitasvir), or NS5B inhibitors (dasabuvir or sofosbuvir), but may potentially impact subsequent treatment with simeprevir or paritaprevir, the later generation HCV protease inhibitors. Thus, use of a regimen that includes simeprevir or paritaprevir is not recommended for retreatment of patients who previously failed therapy that included boceprevir or telaprevir. In contrast, the newer HCV protease inhibitors grazoprevir (coformulated as elbasvir-grazoprevir), glecaprevir (coformulated as glecaprevir-pibrentasvir) and voxilaprevir (coformulated as sofosbuvir-velpatasvir-voxilaprevir) appear to have activity against the typical NS3/4A resistance-associated substitutions encountered in telaprevir- or boceprevir-experienced patients and can be used effectively in such patients. Retreatment must now also consider options for DAA-experienced patients who have previously failed therapy with simeprevir plus sofosbuvir, or a regimen that included an NS5A inhibitor.

## Factors to Consider Prior to Choosing Retreatment Regimen

For persons with chronic hepatitis C genotype 1 infection who have treatment experience, the key factors that influence the choice of the retreatment regimen are (1) the prior regimen used when treatment failure occurred, (2) genotype 1 subtype, (3) the presence or absence of cirrhosis, and (4) cost or insurance considerations.[35] If the genotype 1 subtype is not known, the individual should be treated as genotype 1a. The retreatment of persons with genotype 1 who have decompensated cirrhosis, renal impairment, acute hepatitis C infection, or post-liver transplantation is not addressed here. For individuals with HCV-HIV coinfection, the approach to retreatment is the same as with HCV mono-infection.

## Baseline Resistance Testing

When considering the use of elbasvir-grazoprevir in treatment-experienced persons, note that pretreatment NS5A resistance testing is recommended for all with HCV genotype 1a infection to detect NS5A resistance-associated substitutions at the amino acid positions M28, Q30, L31, or Y93. Just as in treatment-naïve individuals, the presence of one or more of these resistance-associated substitution requires adding ribavirin to the regimen and extending the course of elbasvir-grazoprevir to 16 weeks.[16,36] In addition, for treatment-experienced persons with genotype 1a HCV (with or without cirrhosis) in whom ledipasvir-sofosbuvir is being considered, NS5A resistance-associated substitution testing can provide guidance on an optimal regimen. If greater than 100-fold resistance is present, a different recommended regimen should be considered, or treatment should include weight-based ribavirin for 12 weeks (in patients without cirrhosis) or 24 weeks (in those with cirrhosis).[37]

## AASLD-IDSA HCV Guidance for Retreatment of HCV Genotype 1

The following is a summary of the AASLD-IDSA HCV Guidance for adults with hepatitis C genotype 1a or 1b infection who are treatment experienced and failed prior therapy, including those without cirrhosis and those with compensated cirrhosis.[38,39,40,41,42,43,44] 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 5. AASLD-IDSA HCV Guidance for Genotype 1a: Retreatment Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a 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 Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a 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 Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

*Fixed-dose combination of ombitasvir (25*

+

**Ribavirin**

*1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

mg)/paritaprevir (150 mg)/ritonavir (50 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Simeprevir**  
(150 mg) one tablet once daily for 12 weeks

+

**Sofosbuvir**  
(400 mg) one tablet once daily for 12 weeks

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

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a 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 I](#), [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.

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**  
Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks

+

**Ribavirin**  
1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)

For patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 1a patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 6. AASLD-IDSA HCV Guidance for Genotype 1a: Retreatment Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis^**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

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

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)*

For patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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



^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 1a patients with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

### Table 7. AASLD-IDSA HCV Guidance for Genotype 1b: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

<p><b>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis</b></p> <p><b>Elbasvir-Grazoprevir</b>  <i>Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks</i>                      Rating: <a href="#">Class I</a>, <a href="#">Level A</a></p>
<p><b>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis</b></p> <p><b>Glecaprevir-Pibrentasvir</b>  <i>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks</i>                      *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).                      Rating: <a href="#">Class I</a>, <a href="#">Level A</a></p>
<p><b>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis</b></p> <p><b>Ledipasvir-Sofosbuvir</b>  <i>Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks</i>                      Rating: <a href="#">Class I</a>, <a href="#">Level A</a></p>
<p><b>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis</b></p> <p><b>Sofosbuvir-Velpatasvir</b>  <i>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks</i>                      Rating: <a href="#">Class I</a>, <a href="#">Level A</a></p>

**Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis**

**Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

*\*Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (50 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

**Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis**

**Simeprevir**

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

+

**Sofosbuvir**

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

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

**Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 1b 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 I](#), [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 1b patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 8. AASLD-IDSA HCV Guidance for Genotype 1b: Retreatment Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b**

**Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

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

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

*#\*Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (50 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

#See the warning in the product information regarding risk of serious liver injury when using ombitasvir-paritaprevir-ritonavir plus dasabuvir in patients with cirrhosis

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

<sup>^</sup>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 1b with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 9. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 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](#)

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

**Glecaprevir-Pibrentasvir**

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

Rating: [Class IIa](#), [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 HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

**+ Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

For all genotype 1b patients, and genotype 1a patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Alternative for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet*

**+ Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is*

once daily for 16 weeks

given in two divided doses)

For genotype 1a patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: NS3 protease inhibitor + peginterferon/ribavirin-experienced, genotype 1 patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 10. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 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 HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

**Glecaprevir-Pibrentasvir**

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

Rating: [Class IIa](#), [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 HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

**Ledipasvir-Sofosbuvir + Ribavirin**

Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks

1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)

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

**Alternative for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks

+

**Ribavirin**

1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)

For all genotype 1b patients, and genotype 1a patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Alternative for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks

+

**Ribavirin**

1000 mg if <75 kg or 1200 mg if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)

For genotype 1a patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance

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

<sup>^</sup>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: NS3 protease inhibitor + peginterferon/ribavirin-experienced, genotype 1 patients with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 11. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced,**

Genotype 1 Patients Without Cirrhosis

**Sofosbuvir-Velpatasvir-Voxilaprevir**

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

For genotype 1a patients

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced,**

Genotype 1 Patients Without Cirrhosis

**Glecaprevir-Pibrentasvir**

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

Regardless of HCV genotype 1 subtype

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

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced,**

Genotype 1 Patients Without Cirrhosis

**Sofosbuvir-Velpatasvir**

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

For genotype 1b patients

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

**Alternative for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced,**

Genotype 1 Patients Without Cirrhosis

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

**+ Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

Except in simeprevir failures

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: non-NS5A inhibitor, sofosbuvir-containing regimen-experienced, genotype 1 patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 12. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment**

**Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

Recommended regimens listed by evidence level and alphabetically

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Sofosbuvir-Velpatasvir-Voxilaprevir**

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

For genotype 1a patients

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Glecaprevir-Pibrentasvir**

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

Regardless of genotype 1 subtype

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

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Sofosbuvir-Velpatasvir**

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

For genotype 1b patients

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

<sup>^</sup>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: non-NS5A inhibitor, sofosbuvir-containing regimen-experienced, genotype 1 patients with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 13. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment HCV NS5a Inhibitor DAA-Experienced Genotype 1 Patients, With or Without Compensated Cirrhosis<sup>^</sup>**

**Recommended for HCV NS5a Inhibitor DAA-Experienced Genotype 1 Patients, With or Without Compensated Cirrhosis<sup>^</sup>**

**Sofosbuvir-Velpatasvir-Voxilaprevir**



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

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

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### **Alternative for HCV NS5a Inhibitor DAA-Experienced Genotype 1 Patients, With or Without Compensated Cirrhosis<sup>^</sup>**

#### **Glecaprevir-Pibrentasvir**

*\*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks*

Except NS3/4 protease inhibitor inclusive DAA combination regimens

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

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

<sup>^</sup>For treatment of patients with decompensated cirrhosis, see the AASLD-IDSAs Guidance: Unique Populations—Patients with Decompensated Cirrhosis.

Source: AASLD-IDSAs. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: NS5A inhibitor DAA-experienced genotype 1 patients. [[AASLD-IDSAs Hepatitis C Guidance](#)] - Accessed November 22, 2017.

## **Key Studies for Retreatment of Adults with Genotype 1**

The following key studies support the recommendations in the AASLD-IDSAs HCV Guidance for retreatment of adults with chronic hepatitis C and genotype 1 infection who previously failed therapy.

### **Daclatasvir and Sofosbuvir**

- [ALLY-2](#): In the ALLY-2 trial, treatment-naïve and treatment-experienced adults with HCV genotype 1-4 and HIV coinfection received daclatasvir and sofosbuvir.[[22](#)] All with genotype 1 HCV who were previously treated were assigned to receive 12 weeks of therapy. Overall, SVR12 was achieved in 98% (43 of 44) treatment-experienced participants with genotype 1 infection.
- [AI444040](#): The AI444040 trial had multiple treatment arms of daclatasvir plus sofosbuvir, with or without ribavirin. Enrollment included treatment-naïve and treatment-experienced adults with HCV genotype 1, and treatment-naïve adults with HCV genotype 2 or 3.[[21](#)] The treatment-experienced participants with genotype 1 infection (n=41) received 24 weeks of therapy, with or without ribavirin; 22% (9 of 41) of these patients had cirrhosis. The SVR12 rates for the treatment-experienced participants were 95% (19 of 20) and 100% (21 of 21) for those who received 24 weeks of daclatasvir and sofosbuvir, with and without ribavirin respectively.

### **Elbasvir-Grazoprevir**

- **C-EDGE Treatment-Experienced:** This phase 3 trial enrolled 420 treatment-experienced adults with genotype 1, 4, or 6 to receive the fixed-dose elbasvir-grazoprevir, with or without ribavirin, for 12 or 16 weeks.[36] Overall, 89% of participants enrolled had genotype 1 HCV (54% genotype 1a and 35% genotype 1b). For patients with genotype 1, with 12 weeks of treatment, SVR12 was achieved in 94.7% (89 of 94) in the elbasvir-grazoprevir arm and 94.4% (84 of 89) in the elbasvir-grazoprevir plus ribavirin arm. For patients with genotype 1, with 16 weeks of treatment, SVR12 was obtained in 95.8% (91 of 95) of patients in the elbasvir-grazoprevir arm and in 100% (92 of 92) of those who received elbasvir-grazoprevir plus ribavirin. For patients with genotype 1 who had baseline NS3 resistance-associated substitutions detected, the SVR12 responses were clearly improved by the addition of ribavirin and the best responses were seen with the addition of ribavirin and extension of treatment to 16 weeks.
- **Pooled NS5A Resistance Study of Elbasvir-Grazoprevir:** In this pooled multi-study analysis of baseline NS5A resistance data from the phase 2/3 trials of elbasvir-grazoprevir, among genotype 1a patients, approximately 5% of treatment-naïve and 10% of prior peginterferon plus ribavirin non-responders were found to have at least one NS5A resistance-associated substitution at baseline.[45,46] The resistance-associated substitutions at positions 30, 31 and 93 (detected by population-based sequencing or next-generation sequencing at a sensitivity threshold of 10%) were found to have the greatest impact on treatment efficacy. Genotype 1b participants by comparison were minimally affected by the presence of baseline NS5A resistance-associated substitutions.

### **Glecaprevir-Pibrentasvir**

- **ENDURANCE-1:** In this phase 3 open-label trial, 703 noncirrhotic adults with genotype 1 HCV infection were randomized to receive either 8 or 12 weeks of glecaprevir-pibrentasvir; 38% were treatment-experienced (3 were sofosbuvir experienced and the remainder interferon experienced).[25] Among those enrolled 33 were coinfecting with HIV. The SVR12 rate was 99% for the 8-week arm and 99.7% for the 12-week arm, and the SVR rate remained high in persons with HIV coinfection, prior treatment experience, and baseline resistance-associated substitutions.
- **EXPEDITION-1:** This phase 3, single-arm open-label trial evaluated the safety and efficacy of 12 weeks of glecaprevir-pibrentasvir in 146 adults with compensated cirrhosis and genotype 1, 2, 4, 5, or 6 hepatitis C infection.[26] Sixty percent were genotype 1 patients and 75% were treatment naïve. For participants with genotype 1 infection, 99% (89 of 90) achieved an SRV12. One participant with genotype 1a had a viral relapse at week 8 post-treatment—resistance testing detected a Y93N resistance-associated substitution at baseline and at the time of failure.
- **EXPEDITION-2:** In this open-label, dual-arm phase 3 trial, 137 noncirrhotic adults with HCV (genotype 1-6) and HIV coinfection were assigned 8 weeks of glecaprevir-pibrentasvir and 16 participants with compensated cirrhosis received 12 weeks of glecaprevir-pibrentasvir.[27] Among the 94 participants with genotype 1, 100% achieved an SVR12. All but 10 who enrolled in the study were taking either raltegravir, dolutegravir, or rilpivirine as the anchor drug for HIV antiretroviral therapy.

### **Ledipasvir-Sofosbuvir**

- **ION-2:** In this phase 3 trial, 440 treatment-experienced adults with genotype 1 chronic hepatitis C infection, with or without cirrhosis, received a 12- or 24-week treatment with fixed-dose combination ledipasvir-sofosbuvir, with or without ribavirin.[47] For participants in the 12-week arm, SVR12 was achieved in 94% (102 of 109) treated with ledipasvir-sofosbuvir and in 96% (107 of 111) treated with ledipasvir-sofosbuvir plus ribavirin; with 24 weeks of therapy the SVR12 rates were 99%, with or without ribavirin. Individuals with cirrhosis who received 12 weeks of therapy had lower SVR rates than those without cirrhosis. In addition participants with cirrhosis had higher SVR rates with 24 weeks of ledipasvir-sofosbuvir than

with 12 weeks (100% versus 86%).

- [NIAID Retreatment of Sofosbuvir Failures](#): In this small single-arm study by the NIAID, adults with genotype 1 infection who had relapsed with prior therapy with 24 weeks of sofosbuvir and ribavirin in the SPARE study were subsequently treated with 12 weeks of ledipasvir-sofosbuvir and 100% (14 of 14) achieved an SVR12.[48]
- [Retreatment of Sofosbuvir Failures from prior Clinical Trials](#): This phase 2 trial enrolled adults with genotype 1 chronic HCV who failed a sofosbuvir-containing regimen while participating in a phase 2 or 3 Gilead-sponsored clinical trial.[49] In a 12-week treatment arm, study participants received retreatment with ledipasvir-sofosbuvir plus ribavirin. The study design permitted enrollment of individuals with compensated cirrhosis. Preliminary results from this 12-week group showed an SVR12 rate of 98% (50 of 51).

### **Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

- [SAPPHIRE-II](#): In this phase 3 trial, investigators examined the safety and efficacy of a 12-week course of ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin in adults with chronic hepatitis C infection, genotype 1, without cirrhosis, who had previously failed treatment with peginterferon and ribavirin.[50] Among participants who received ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin, 96% (286 of 297) achieved an SVR12, with similar results observed with genotype 1a (96%) and 1b (97%). This study shows a 12-week course of ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin is highly effective in persons with genotype 1 HCV who previously failed treatment with peginterferon and ribavirin.
- [TUROQUOISE-II](#): This phase 3 trial enrolled treatment-naïve and treatment-experienced adults with chronic hepatitis C infection, genotype 1, and Child-Turcotte-Pugh class A cirrhosis. Participants received ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin regimen for 12 weeks (Group A) or 24 weeks (Group B).[31] The overall SVR12 rates were 92% in Group A (191 of 208) and 96% (165 of 172) in Group B. For those with genotype 1a, SVR12 rates were 89% (124 of 140) for group A 94% (114 of 121) for group B. For participants with genotype 1b, SVR12 rates were 99% (67 of 68) in Group A and 100% (50 of 51) in Group B. There was a clinically meaningful difference in the SVR12 between the 12-week and 24-week treatment groups in patients with Genotype 1a infection and prior null response (80% versus 92.9%), which suggests that individuals in this subgroup probably benefit from extending therapy to 24 weeks.

### **Simeprevir and Sofosbuvir**

- [COSMOS](#): In this open-label, phase 2a trial, investigators enrolled treatment-naïve and prior null responder adults with genotype 1 to receive the combination of simeprevir plus sofosbuvir for 12 or 24 weeks, with or without ribavirin.[51] All participants in cohort 1 were prior null responders to peginterferon and ribavirin and had Metavir fibrosis scores F0 to F2. Cohort 2 included null responders (54%) and treatment-naïve adults (46%) with Metavir fibrosis scores F3 to F4. The SVR rates ranged from 79 to 93% in Cohort 1 and 93 to 100% in Cohort 2.
- [SIRIUS](#): In this phase 2, double-blind trial, treatment-experienced adults with genotype 1 HCV and compensated cirrhosis received either ledipasvir-sofosbuvir plus ribavirin for 12 weeks or ledipasvir-sofosbuvir without ribavirin for 24 weeks.[52] All participants had previously sequentially failed dual therapy with peginterferon and ribavirin and triple therapy with peginterferon and ribavirin and an NS3/4A protease inhibitor. The SVR12 rates were very high in both groups: 96% in the 12-week group and 97% in the 24-week group. The study provides supportive data for the use of a 12-week course of ledipasvir-sofosbuvir plus ribavirin in patients with compensated cirrhosis, if they can tolerate ribavirin.
- [OPTIMIST-1](#): In this randomized, phase 3, open-label trial, investigators compared an 8-week versus 12-week regimen of simeprevir plus sofosbuvir in HCV genotype 1, treatment-naïve

and treatment-experienced adults without cirrhosis.[32] Overall, participants achieved better SVR12 rates in the 12-week arm (97% [150 of 155]) than in the 8-week arm (83% [128 of 155]). In the treatment-experienced participants, the SVR12 rates with the 12-week regimen were superior to the 8-week regimen (95% versus 77%). This study demonstrates the all-oral 12-week regimen of simeprevir plus sofosbuvir is highly effective and well tolerated in treatment-naïve and treatment-experienced HCV genotype 1 patients without cirrhosis.

- **OPTIMIST-2:** This randomized, phase 3, open-label, single-arm trial examined the effectiveness and safety of a 12-week treatment course with simeprevir plus sofosbuvir in treatment-naïve or treatment-experienced adults with chronic HCV genotype 1 and compensated cirrhosis.[33] Overall, 83% (86 of 103) persons treated with simeprevir plus sofosbuvir achieved an SVR12. Among the treatment-experienced participants, 79% (42 of 53) had an SVR12. In the combined data for the 72 treatment-naïve and treatment-experienced individuals with genotype 1a infection, the SVR12 rates were higher in the group without the baseline Q80K mutation than those with the baseline Q80K mutation (92% versus 74%). This study demonstrates that the all-oral 12-week regimen of simeprevir plus sofosbuvir is moderately effective in treatment-experienced adults with cirrhosis and HCV genotype 1, but individuals with genotype 1a and a baseline Q80K mutation had lower SVR rates.

## HCV Genotype 1: Treatment Regimens Under Study

### Treatment Regimens Under Study for Persons with HCV Genotype 1

Since multiple DAA regimens are now available that are highly effective against HCV genotype 1 in treatment-naïve and treatment-experienced adults, the incentive for development of future treatment options has diminished. Nevertheless, several agents are currently under investigation for the treatment of hepatitis C genotype 1 infection.

- **Grazoprevir-Ruzasvir-Uprifosbuvir (MK-3682)**: A new 3-drug DAA combination that includes the protease inhibitor grazoprevir with a novel NS5A inhibitor, ruzasvir, and a novel NS5B nucleotide polymerase inhibitor, uprifosbuvir, is currently under investigation for treatment of genotype 1 adults who are treatment-naïve or DAA-experienced.[[53](#),[54](#),[55](#)]
- **AL-335 plus Odalasvir with or without Simeprevir**: AL-355, an investigational uridine-based nucleotide analogue NS5B inhibitor, is currently being studied in combination with odalasvir, a novel NS5A inhibitor, with or without simeprevir in noncirrhotic, treatment-naïve, genotype 1 adults for 6 or 8 weeks.

## Summary Points

- For initial therapy of treatment-naïve genotype 1a patients without cirrhosis, four coformulated regimens with similar efficacy are recommended in the AASLD-IDSa guidance: (a) elbasvir-grazoprevir (12 weeks, if no key resistance-associated substitutions are detected on pretreatment NS5A testing); (b) glecaprevir-pibrentasvir (8 weeks); (c) ledipasvir-sofosbuvir (8 or 12 weeks); or (d) sofosbuvir-velpatasvir (12 weeks).
- For initial therapy of treatment-naïve genotype 1a patients with compensated cirrhosis, four 12-week regimens with similar efficacy are recommended: (a) elbasvir-grazoprevir (if no key resistance-associated substitutions are detected on pretreatment NS5A testing); (b) glecaprevir-pibrentasvir; (c) ledipasvir-sofosbuvir; or (d) sofosbuvir-velpatasvir.
- For initial therapy of treatment-naïve genotype 1b patients without cirrhosis, the recommended regimens are the same as for genotype 1a without cirrhosis, except that baseline NS5A resistance testing is not required for genotype 1b patients treated with elbasvir-grazoprevir since treatment of HCV genotype 1b with elbasvir-grazoprevir is not significantly impacted by baseline NS5A resistance-associated substitutions.
- For initial therapy of treatment-naïve genotype 1b patients with compensated cirrhosis, the recommended regimens are the same as for genotype 1a with compensated cirrhosis, except that baseline NS5A resistance testing is not required for genotype 1b patients treated with elbasvir-grazoprevir since treatment of HCV genotype 1b with elbasvir-grazoprevir is not significantly impacted by baseline NS5A resistance-associated substitutions.
- For retreatment of patients with genotype 1a without cirrhosis who previously failed therapy with peginterferon and ribavirin, the following regimens are recommended: (a) elbasvir-grazoprevir (12 weeks), (b) glecaprevir-pibrentasvir (8 weeks), (c) ledipasvir-sofosbuvir (12 weeks) or (d) sofosbuvir-velpatasvir (12 weeks).
- For retreatment of genotype 1a patients with compensated cirrhosis who previously failed therapy with peginterferon and ribavirin, three 12-week regimens with similar efficacy are recommended: (a) elbasvir-grazoprevir (if no key resistance-associated substitutions are detected on pretreatment NS5A testing); (b) sofosbuvir-velpatasvir; or (c) glecaprevir-pibrentasvir.
- For retreatment of patients with genotype 1b without cirrhosis who previously failed therapy with peginterferon and ribavirin, the same 12-week regimens are recommended as for initial treatment in genotype 1b patients without cirrhosis, except that baseline NS5A resistance testing is not required for genotype 1b patients treated with elbasvir-grazoprevir.
- For retreatment of genotype 1b patients with compensated cirrhosis who previously failed therapy with peginterferon and ribavirin, three 12-week regimens are recommended: (a) elbasvir-grazoprevir; (b) sofosbuvir-velpatasvir; or (c) glecaprevir-pibrentasvir.
- In patients with HCV genotype 1a or 1b infection without cirrhosis who failed an NS3 protease-inhibitor (telaprevir, boceprevir or simeprevir) with peginterferon and ribavirin, three 12-week regimens are recommended: (a) ledipasvir-sofosbuvir; (b) sofosbuvir-velpatasvir; or (c) glecaprevir-pibrentasvir. For such patients with compensated cirrhosis, two 12-week regimens are recommended: (a) sofosbuvir-velpatasvir or (b) glecaprevir-pibrentasvir.
- In patients with HCV genotype 1a or 1b infection who previously failed a sofosbuvir-containing regimen (without an NS5A inhibitor), three 12-week regimens are recommended: (a) sofosbuvir-velpatasvir-voxilaprevir for genotype 1a; (b) glecaprevir-pibrentasvir for genotype 1a or 1b; or (c) sofosbuvir-velpatasvir for genotype 1b; these same regimens are recommended for patients without cirrhosis or with compensated cirrhosis.
- In patients with HCV genotype 1 (1a or 1b), with or without compensated cirrhosis, who are DAA-experienced with a prior NS5A-containing regimen, the recommended regimen is sofosbuvir-velpatasvir-voxilaprevir for 12 weeks.

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## Figures

**Figure 1 Estimated Cost of Medication Regimens Used to Treat Genotype 1a Chronic HCV, Without Cirrhosis**

This figure shows the approximate cost of different regimens used for treatment-naïve patients with genotype 1a chronic HCV. Cost estimates based on available wholesale acquisition cost. The regimens listed are recommended regimens for patients without cirrhosis.

Estimated Wholesale Acquisition Cost (WAC)	
Recommended Regimens for GT1a HCV, without Cirrhosis	
Regimens and Duration of Therapy	Cost of Regimen
*Elbasvir-Grazoprevir x 12 weeks	\$54,600
Glecaprevir-Pibrentasvir x 8 weeks	\$26,400
^Ledipasvir-Sofosbuvir x 8 weeks	\$63,000
Ledipasvir-Sofosbuvir x 12 weeks	\$94,500
Sofosbuvir-Velpatasvir x 12 weeks	\$74,760

\*This 12-week regimen is for patients without baseline NS5A resistance-associated substitutions (at amino acid positions 28, 30, 31, or 93) for elbasvir  
 ^This 8-week regimen is appropriate only for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL



**Figure 2 Estimated Cost of Medication Regimens Used to Treat Genotype 1a Chronic HCV, With Compensated Cirrhosis**

This figure shows the approximate cost of different regimens used for treatment-naïve patients with genotype 1a chronic HCV. Cost estimates based on available wholesale acquisition cost. The regimens listed are recommended regimens for patients with compensated cirrhosis.

<b>Estimated Wholesale Acquisition Cost (WAC)</b>	
<b>Recommended Regimens for GT1a HCV, with Compensated Cirrhosis</b>	
<b>Regimens and Duration of Therapy</b>	<b>Cost of Regimen</b>
*Elbasvir-Grazoprevir x 12 weeks	\$54,600
Glecaprevir-Pibrentasvir x 12 weeks	\$39,600
Ledipasvir-Sofosbuvir x 12 weeks	\$94,500
Sofosbuvir-Velpatasvir x 12 weeks	\$74,760

\*This 12-week regimen is for patients without baseline NS5A resistance-associated substitutions (at amino acid positions 28, 30, 31, or 93) for elbasvir  
 ^This 8-week regimen is appropriate only for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL

**Figure 3 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		

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

Recommended and alternative regimens listed by evidence level and alphabetically

### Recommended for Treatment-Naïve Genotype 1a Patients Without Cirrhosis

#### Elbasvir-Grazoprevir

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

### Recommended for Treatment-Naïve Genotype 1a 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 1a Patients Without Cirrhosis

#### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

### Recommended for Treatment-Naïve Genotype 1a Patients Without Cirrhosis

#### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 8 weeks*

For patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL.

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

### Recommended for Treatment-Naïve Genotype 1a 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 1a Patients Without Cirrhosis

**Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

*\*Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

**Alternative for Treatment-Naïve Genotype 1a Patients Without Cirrhosis**

**Simeprevir**

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

+

**Sofosbuvir**

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

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

**Alternative for Treatment-Naïve Genotype 1a 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 I, 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 detailed information.

**Alternative for Treatment-Naïve Genotype 1a Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)*

For patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

Note: The ribavirin daily dose is given in two divided doses.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 1a without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

## Table 2. AASLD-IDSA HCV Guidance for Genotype 1a: Initial Treatment Treatment-Naïve Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>

Recommended and alternative regimens listed by evidence level and alphabetically

### Recommended for Treatment-Naïve Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>

#### Elbasvir-Grazoprevir

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

### Recommended for Treatment-Naïve Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>

#### Glecaprevir-Pibrentasvir

*\*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 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 1a Patients With Compensated Cirrhosis<sup>^</sup>

#### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

### Recommended for Treatment-Naïve Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>

#### 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 1a Patients With Compensated Cirrhosis<sup>^</sup>

#### Elbasvir-Grazoprevir

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks*

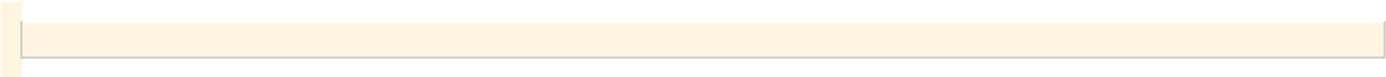
+

#### Ribavirin

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)*

For patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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



^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-naive genotype 1a with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

### Table 3. AASLD-IDSA HCV Guidance for Genotype 1b: Initial Treatment Treatment-Naïve Genotype 1b Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically.

#### Recommended for Treatment-Naïve Genotype 1b Patients Without Cirrhosis

##### Elbasvir-Grazoprevir

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

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

#### Recommended for Treatment-Naïve Genotype 1b 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 1b Patients Without Cirrhosis

##### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

#### Recommended for Treatment-Naïve Genotype 1b Patients Without Cirrhosis

##### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 8 weeks*

For patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL.

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

#### Recommended for Treatment-Naïve Genotype 1b 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 1b Patients Without Cirrhosis

##### Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir

*\*Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

**Alternative for Treatment-Naïve Genotype 1b Patients Without Cirrhosis**

**Simeprevir**

(150 mg) one tablet once daily for 12 weeks

+

**Sofosbuvir**

(400 mg) one tablet once daily for 12 weeks

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

**Alternative for Treatment-Naïve Genotype 1b 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 I](#), [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 detailed information.

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naïve genotype 1b without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 21, 2017.



## Table 4. AASLD-IDSA HCV Guidance for Genotype 1b: Initial Treatment Treatment-Naïve Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>

Recommended and alternative regimens listed by evidence level and alphabetically.

### Recommended for Treatment-Naïve Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>

#### Elbasvir-Grazoprevir

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

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

### Recommended for Treatment-Naïve Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>

#### Glecaprevir-Pibrentasvir

*\*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 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 1b Patients With Compensated Cirrhosis<sup>^</sup>

#### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

### Recommended for Treatment-Naïve Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>

#### 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 1b Patients With Compensated Cirrhosis<sup>^</sup>

#### Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir

*##Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

#See the warning in the product information regarding risk of serious liver injury when using ombitasvir-paritaprevir-ritonavir with or without dasabuvir in patients with cirrhosis.

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 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. Initial treatment of HCV infection: treatment-naive genotype 1b with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 5. AASLD-IDSA HCV Guidance for Genotype 1a: Retreatment Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a 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 Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a 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 Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

+

**Ribavirin**

*1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks (the daily dose is given in*

Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (50 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Simeprevir** (150 mg) one tablet once daily for 12 weeks + **Sofosbuvir** (400 mg) one tablet once daily for 12 weeks

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

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a 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 I, 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.

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients Without Cirrhosis**

**Elbasvir-Grazoprevir** Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks + **Ribavirin** 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)

For patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 1a patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 6. AASLD-IDSA HCV Guidance for Genotype 1a: Retreatment Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

For patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

**+ Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

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

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1a Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

**Ribavirin**

Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks + 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)

For patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; these NS5A RASs include genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

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

Source: AASLD-IDS A. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon/ribavirin-experienced, genotype 1a patients with compensated cirrhosis. [[AASLD-IDS A Hepatitis C Guidance](#)] - Accessed November 22, 2017.

## Table 7. AASLD-IDSA HCV Guidance for Genotype 1b: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

### Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis

#### Elbasvir-Grazoprevir

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

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

### Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis

#### Glecaprevir-Pibrentasvir

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

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

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

### Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis

#### Ledipasvir-Sofosbuvir

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

### Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 1b 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 1b Patients Without Cirrhosis

#### Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir

*\*Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (50 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 mg).

**Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis**

**Simeprevir**

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

+

**Sofosbuvir**

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

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

**Alternative for Peginterferon plus Ribavirin-Experienced, Genotype 1b 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 I](#), [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 1b patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.



**Table 8. AASLD-IDSA HCV Guidance for Genotype 1b: Retreatment Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

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

**Recommended for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**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 Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

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

**Alternative for Peginterferon plus Ribavirin Treatment-Experienced, Genotype 1b Patients With Compensated Cirrhosis<sup>^</sup>**

**Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir**

*#\*Fixed-dose combination of ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (50 mg) once daily plus dasabuvir (250 mg) twice daily for 12 weeks*

#See the warning in the product information regarding risk of serious liver injury when using ombitasvir-paritaprevir-ritonavir plus dasabuvir in patients with cirrhosis

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

Note: \*Alternatively, the extended-release regimen can be used and this consists of a fixed-dose combination of dasabuvir (600 mg)/ombitasvir (25 mg)/paritaprevir (150 mg)/ritonavir (100 mg). The

extended-release regimen is taken as 3 extended release tablets once daily; each fixed-dose tablet contains dasabuvir (200 mg)/ombitasvir (8.33 mg)/paritaprevir (50 mg)/ritonavir (33.33 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: peginterferon/ribavirin-experienced, genotype 1b with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 9. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**  
**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

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

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 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](#)

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**  
**Glecaprevir-Pibrentasvir**

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

Rating: [Class IIa](#), [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 HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

**+ Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

For all genotype 1b patients, and genotype 1a patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Alternative for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)*

For genotype 1a patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: NS3 protease inhibitor + peginterferon/ribavirin-experienced, genotype 1 patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 10. AASLD-IDS A HCV Guidance for Genotype 1: Retreatment HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 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 HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

**Glecaprevir-Pibrentasvir**

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

Rating: [Class IIa](#), [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 HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

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

**Alternative for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis^**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

For all genotype 1b patients, and genotype 1a patients without baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

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

**Alternative for HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Elbasvir-Grazoprevir**

*Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks*

+

**Ribavirin**

*1000 mg if <75 kg or 1200 mg if ≥75 kg for 16 weeks (the daily dose is given in two divided doses)*

For genotype 1a patients with baseline NS5A resistance-associated substitutions (RASs) for elbasvir; the RASs includes genotype 1a RASs at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance

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

<sup>^</sup>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: NS3 protease inhibitor + peginterferon/ribavirin-experienced, genotype 1 patients with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 11. AASLD-IDS A HCV Guidance for Genotype 1: Retreatment Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis**

Recommended and alternative regimens listed by evidence level and alphabetically

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis**

**Sofosbuvir-Velpatasvir-Voxilaprevir**

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

For genotype 1a patients

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis**

**Glecaprevir-Pibrentasvir**

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

Regardless of HCV genotype 1 subtype

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

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis**

**Sofosbuvir-Velpatasvir**

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

For genotype 1b patients

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

**Alternative for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis**

**Ledipasvir-Sofosbuvir**

*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*

+

**Ribavirin**

*1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks (the daily dose is given in two divided doses)*

Except in simeprevir failures

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

Source: AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: non-NS5A inhibitor, sofosbuvir-containing regimen-experienced, genotype 1 patients without cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.



**Table 12. AASLD-IDSA HCV Guidance for Genotype 1: Retreatment Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

Recommended regimens listed by evidence level and alphabetically

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Sofosbuvir-Velpatasvir-Voxilaprevir**

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

For genotype 1a patients

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Glecaprevir-Pibrentasvir**

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

Regardless of genotype 1 subtype

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

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

**Recommended for Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis<sup>^</sup>**

**Sofosbuvir-Velpatasvir**

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

For genotype 1b patients

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

<sup>^</sup>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: non-NS5A inhibitor, sofosbuvir-containing regimen-experienced, genotype 1 patients with compensated cirrhosis. [[AASLD-IDSA Hepatitis C Guidance](#)] - Accessed November 22, 2017.

**Table 13. AASLD-IDSa HCV Guidance for Genotype 1: Retreatment HCV NS5a Inhibitor DAA-Experienced Genotype 1 Patients, With or Without Compensated Cirrhosis<sup>^</sup>**

**Recommended for HCV NS5a Inhibitor DAA-Experienced Genotype 1 Patients, With or Without Compensated Cirrhosis<sup>^</sup>**

**Sofosbuvir-Velpatasvir-Voxilaprevir**

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

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

**Alternative for HCV NS5a Inhibitor DAA-Experienced Genotype 1 Patients, With or Without Compensated Cirrhosis<sup>^</sup>**

**Glecaprevir-Pibrentasvir**

*\*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 16 weeks*

Except NS3/4 protease inhibitor inclusive DAA combination regimens

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

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

<sup>^</sup>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: NS5a inhibitor DAA-experienced genotype 1 patients. [[AASLD-IDSa Hepatitis C Guidance](#)] - Accessed November 22, 2017.

