

Treatment of HCV Genotype 1

This is a PDF version of the following document:

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

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

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

Introduction

Background: In the United States, genotype 1 HCV is the most common infection, accounting for approximately 70 to 75% of all hepatitis C infections. Accordingly, treatment of genotype 1 has the most extensive data and highest clinical relevance for hepatitis C treatment issues in the United States. Genotype 1 infection has been historically difficult to treat, but multiple recent studies have shown SVR rates greater than 90% in these genotype 1 patients using well-tolerated, all-oral regimens consisting of new direct-acting antiviral agents. The use of these direct-acting antiviral agents has been complicated by the high price of therapy. For example, the cost of preferred regimens as recommended in the 2016 American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD/IDSA) guidance for initial therapy of patients with genotype 1a or 1b (without cirrhosis) ranges from approximately \$55,000 to \$150,000 ([Figure 1](#)) and ([Figure 2](#)). The following discussion regarding initial treatment and retreatment of patients with genotype 1a or 1b chronic hepatitis C assumes the patient and their clinician have already made the decision to initiate hepatitis C therapy.

Medications used to Treat Hepatitis C: 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. 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.

Genotype 1: Initial Treatment

Background: The treatment landscape for patients with genotype 1 chronic hepatitis C infection has rapidly changed in recent years. Historically, genotype 1 hepatitis C has been 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). 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. Since 2015, the standard of care for genotype 1 consists of all-oral therapy with a combination of direct-acting antiviral agents (DAAs). In 2016, multiple all-oral 12-week regimens are recommended for the treatment of HCV genotype 1: fixed-dose elbasvir-grazoprevir, fixed-dose ledipasvir-sofosbuvir, fixed-dose ombitasvir-paritaprevir-ritonavir and dasabuvir, simeprevir plus sofosbuvir, fixed-dose sofosbuvir-velpatasvir, and daclatasvir plus sofosbuvir. All of these regimens are safe and highly effective.

Factors to Consider Prior to Choosing Initial Treatment Regimen: For treatment-naive patients chronically infected with genotype 1 hepatitis C, three key factors influence the choice and duration of therapy: genotype 1 subtype (1a or 1b), cirrhosis status, and prior treatment experience. If the genotype 1 subtype is not known, the patient should be treated as genotype 1a. In general, the baseline HCV RNA value does not influence the treatment choice or duration. With ledipasvir-sofosbuvir, however, a post-hoc analysis from the ION-3 trial in treatment-naive patients without cirrhosis noted that patients with a baseline HCV RNA level less than 6 million IU/mL had similar relapse rates using 8 or 12 weeks of therapy. Additional data from the HCV-TARGET registry and the Veterans Affairs National Healthcare System demonstrated comparable high SVR rate of 94 to 98% for patients with either 8 or 12 weeks of ledipasvir-sofosbuvir among non-cirrhotic patients with baseline HCV RNA levels less than 6 million IU/mL. Drug interactions may also influence the choice of therapy, particularly for HIV-coinfected patients. The management of genotype 1 patients with decompensated cirrhosis, renal impairment, HIV coinfection, acute hepatitis C infection, or post-liver transplantation can impact choice of treatment regimens and/or duration of therapy and is not addressed in this lesson.

Baseline Resistance Testing: When considering the use of elbasvir-grazoprevir, pre-treatment NS5A resistance testing is recommended for patients with HCV genotype 1a to detect the presence of virus with NS5A resistance-associated variants (RAVs) at the amino acid positions M28, Q30, L31, or Y93. The presence of one or more of these high-fold change RAVs requires adding ribavirin to the regimen and extending the course of elbasvir-grazoprevir to 16 weeks. Genotypic resistance testing is commercially available through several laboratories and typically costs less than \$1000. The significantly lower cost of elbasvir-grazoprevir compared with other DAAs may lower the barrier to this pre-treatment testing. When considering the use of simeprevir plus sofosbuvir in patients with genotype 1a and compensated cirrhosis, baseline NS3/4A resistance testing should be performed to determine whether the Q80K mutation is present; in this situation, simeprevir plus sofosbuvir should only be used in patients in whom no Q80K polymorphism is detected.

AASLD/IDSA Guidance (see [Initial Treatment of HCV Infection](#)): The following is a summary of joint recommendations issued by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). The AASLD/IDSA recommendations summarized below are for patients with hepatitis C genotype 1a and 1b infection who will receive initial treatment. The recommended four regimens for genotype 1a or 1b are listed by groups by level of evidence, then in alphabetical order. Ultimately, the choice of a particular regimen will be influenced by cost, insurance coverage, pill burden, potential drug interactions, use of ribavirin, relevant comorbid conditions, and the patient and provider preferences. Note the AASLD/IDSA recommended weight-based ribavirin dosing, when used with elbasvir-grazoprevir, is different than the weight-based recommended ribavirin dosing in the elbasvir-grazoprevir prescribing information.

Genotype 1a: Initial Treatment

Table 1. Treatment-Naive Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for 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 use only if patient has NO baseline high fold-change NS5A RAVs for elbasvir detected; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

Recommended for 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 Genotype 1a patients without Cirrhosis

Ombitasvir-Pa + ritaprevir- Ritonavir and Dasabuvir

*Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75
mg)/ritonavir (50
mg) two tablets
once daily plus
dasabuvir (250 mg)
one tablet twice
daily for 12 weeks*

Genotype 1: Retreating Persons who Failed Prior Therapy

Background: New interferon-free treatment options have markedly improved the SVR12 response rates in patients with prior treatment experience, with SVR12 rates greater than 90% (compared to historic SVR12 rates of 30 to 60% with triple therapy consisting of peginterferon, ribavirin, and either telaprevir or boceprevir). Prior failure with a regimen that included an NS3/4A protease inhibitor (boceprevir or telaprevir) does not impact subsequent therapy with sofosbuvir, ledipasvir, ombitasvir, or dasabuvir, 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 new HCV protease inhibitor grazoprevir (coformulated in elbasvir-grazoprevir) appears to have activity against the typical NS3/4A RAVs encountered in telaprevir or boceprevir-experienced patients and can be used effectively in such patients. Retreatments now must consider options for patients who have previously failed therapy with simeprevir plus sofosbuvir, as well as failure with a regimen that included an NS5A inhibitor.

Factors to Consider Prior to Choosing Retreatment Regimen: For patients with chronic hepatitis C genotype 1 infection who have treatment experience, the primary factors that determine the recommended retreatment regimen and duration of treatment are the prior regimen used when treatment failure occurred, genotype 1 subtype, and the presence of cirrhosis. If the genotype 1 subtype is not known, the patient should be treated as genotype 1a. Ultimately, the choice of a particular regimen will be influenced by cost, insurance coverage, pill burden, potential drug interactions, use of ribavirin, relevant comorbid conditions, and the patient and provider preferences. The retreatment of genotype 1 patients with decompensated cirrhosis, renal impairment, HIV coinfection, acute hepatitis C infection, or post-liver transplantation is not addressed here.

Baseline Resistance Testing: When considering the use of elbasvir-grazoprevir, note that pre-treatment NS5A resistance testing is recommended for patients with HCV genotype 1a infection to detect the presence of virus with NS5A resistance-associated polymorphisms at the amino acid positions M28, Q30, L31, or Y93. The presence of one or more of these high-fold change RAVs requires adding ribavirin to the regimen and extending the course of elbasvir-grazoprevir to 16 weeks. In addition, NS3/4A resistance testing is recommended in treatment-experienced genotype 1a patients with cirrhosis if simeprevir is being considered as part of the treatment regimen, since detection of the Q80K mutation would exclude the use of simeprevir in this situation.

AASLD/IDSA Guidance (see [Retreatment of Persons in Whom Prior Therapy has Failed](#)): The following is a summary of recommendations issued by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). The AASLD/IDSA recommendations listed below are for patients with hepatitis C genotype 1 infection who are treatment experienced and previously failed therapy.

[\(Table 3\)](#)

[\(Table 4\)](#)

[\(Table 5\)](#)

[\(Table 6\)](#)

[\(Table 7\)](#)

[\(Table 8\)](#)

Key Studies to Support Recommendations: The following key studies support the

recommendations for retreatment of patients with chronic hepatitis C and genotype 1 infection who previously failed therapy. Click on the study name (blue) to see more details and summary PowerPoint slides.

- [ALLY-2](#): In the ALLY-2 trial, treatment-naïve and treatment-experienced patients with HCV genotype 1-4 and HIV coinfection received daclatasvir and sofosbuvir. All previously treated genotype 1 patients were assigned to receive 12 weeks of therapy. Overall, SVR12 was achieved in 43 (98%) of 44 treatment-experienced patients with genotype 1 infection.
- [A1444040](#): The A1444040 trial had multiple treatment arms of daclatasvir and sofosbuvir, with or without ribavirin. Enrollment included treatment-naïve and treatment-experienced patients with genotype 1 and treatment-naïve with genotype 2 or 3. The treatment-experienced patients with genotype 1 infection (n=41) received 24 weeks of therapy, with or without ribavirin; 9 (22%) of 41 of these patients had cirrhosis. The SVR12 rates were 100% (21/21 patients) and 95% (19/20 patients) for 24 weeks of daclatasvir and sofosbuvir, without and with ribavirin respectively.
- [C-EDGE Treatment-Experienced](#): This phase 3 trial enrolled 420 patients with genotype 1, 4, or 6 to receive a 12-week course of the fixed-dose elbasvir-grazoprevir, with or without ribavirin, for 12 or 16 weeks. Preliminary results suggest excellent SVR12 rates in patients with genotype 1 infection, regardless of treatment duration or addition of ribavirin.
- **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/ribavirin non-responder were found to have at least one NS5A resistance-associated variant (RAV) at baseline. The RAVs 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 patients by comparison were minimally affected by the presence of baseline NS5A RAVs.
- [ION-2](#): In this phase 3 trial, 440 treatment-experienced patients 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. The SVR12 rate with 12 weeks of ledipasvir-sofosbuvir was 94% without ribavirin and 96% with ribavirin; with 24 weeks of therapy the SVR12 rates were 99%, with or without ribavirin. Patients with cirrhosis who received 12 weeks of therapy had lower SVR rates than patients without cirrhosis. In addition patients with cirrhosis had higher SVR rates with 24 weeks of ledipasvir-sofosbuvir than with 12 weeks (100% versus 86%).
- [SAPPHIRE-II](#): In this phase 3 trial, investigators examined the safety and efficacy of ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin in patients with chronic hepatitis C infection, genotype 1, without cirrhosis, who had previously failed treatment with peginterferon and ribavirin. Among patients who received ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin, 96.3% achieved an SVR12, with similar results observed with genotype 1a (96.0%) and 1b (96.7%).
- [TURQUOISE-II](#): This phase 3 trial enrolled treatment-naïve and treatment-experienced patients with chronic hepatitis C infection, genotype 1, and Child-Turcotte-Pugh class A cirrhosis. Patients received ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin regimen for 12 weeks (Group A) or 24 weeks (Group B). The overall SVR12 rates were 92% in Group A and 96% in Group B. For patients with genotype 1a, SVR12 rates were 89% and 94% for groups A and B respectively. For patients with genotype 1b, SVR12 rates were 99% in Group A and 100% 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 patients in this subgroup will likely benefit from extending therapy to 24 weeks.
- [COSMOS](#): In this open-label, phase 2a trial, investigators enrolled treatment-naïve and prior null responder patients with genotype 1 to receive the combination of sofosbuvir plus simeprevir for 12 or 24 weeks, with or without ribavirin. All patients 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%) with and treatment-naive patients (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 patients with genotype 1 HCV and compensated cirrhosis received either ledipasvir-sofosbuvir plus ribavirin for 12 weeks or ledipasvir-sofosbuvir without ribavirin for 24 weeks. All patients 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.
- [NIAID Retreatment of Sofosbuvir Failures](#): In this small single-arm study by the NIAID, 14 patients 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 all 14 achieved an SVR12.
- [Retreatment of Sofosbuvir Failures from prior Clinical Trials](#): This phase 2 trial enrolled patients with genotype 1 chronic HCV who failed a sofosbuvir-containing regimen while participating in a phase 2 or 3 Gilead-sponsored clinical trial. In the 12-week treatment arm, patients received retreatment with ledipasvir-sofosbuvir plus ribavirin. The study design permitted enrollment of patients with compensated cirrhosis. Preliminary results from this 12-week group showed an SVR12 rate of 98% (50 of 51). The other treatment arms, which involve 24 weeks of treatment of ledipasvir-sofosbuvir, with or without ribavirin, are currently ongoing.
- [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-naive and treatment-experienced patients without cirrhosis. Overall, SVR12 rates were better in the 12-week arm 150 (97%) of 155 than in the 8-week arm 128 (83%) of 155. In the treatment-experienced patients, 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-naive 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-naive or treatment-experienced patients with chronic HCV genotype 1 and compensated cirrhosis. Overall, treatment with simeprevir plus sofosbuvir resulted in an SVR12 in 86 (83%) of 103 patients. Treatment-experienced patients had an SVR12 rate of 79%. In the combined data for treatment-naive and treatment-experienced patients 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 patients with cirrhosis and HCV genotype 1, but patients with genotype 1a and the baseline Q80K mutation had lower SVR rates.

Genotype 1: Future Treatment Options

Options for Treatment of HCV Genotype 1 in Future: Several agents are currently under investigation for hepatitis C genotype 1 infection.

- **Voxilaprevir (formerly GS-9857):** The investigational NS3/4A protease inhibitor voxilaprevir is currently under study in co-formulated combination with sofosbuvir-velpatasvir, with particular interest in use as short-duration treatment and as salvage therapy for DAA treatment failures.
- **ABT-493 plus ABT-530:** The coformulated combination of ABT-493 (NS3/4A protease inhibitor) plus ABT-530 (NS5A inhibitor) is a pangenotypic non-ribavirin-containing regimen currently under study as both an 8-week regimen for genotype 1 patients without cirrhosis as well as a 12-week salvage regimen for DAA-experienced patients.
- **MK-3682 and MK-8408:** The investigational agents MK-3682, an NS5B inhibitor, and MK-8408, a second-generation NS5A inhibitor, are being evaluated in a variety of triple combinations with either grazoprevir or elbasvir as an 8-week regimen in genotype 1, 2 or 3 infection..

Summary Points

- New direct-acting interferon-free regimens are now the standard of care for the treatment of chronic hepatitis C genotype 1 infection.
- For initial therapy of treatment-naïve genotype 1a patients without cirrhosis, six 12-week regimens with similar efficacy are recommended in the AASLD/IDSA guidance (a) elbasvir-grazoprevir; (b) ledipasvir-sofosbuvir, (c) ombitasvir-paritaprevir-ritonavir and dasabuvir plus ribavirin; (d) simeprevir plus sofosbuvir; (e) sofosbuvir-velpatasvir; and (f) daclatasvir plus sofosbuvir. All regimens except the daclatasvir plus sofosbuvir have a rating of Class 1, Level A.
- For initial therapy of treatment-naïve genotype 1a patients with compensated cirrhosis, three 12-week regimens with similar efficacy are recommended: (a) elbasvir-grazoprevir, (b) ledipasvir-sofosbuvir, and (c) sofosbuvir-velpatasvir.
- When treating genotype 1a patients with elbasvir-grazoprevir, baseline NS5A resistance testing is required to identify the RAVs at amino acid positions M28, Q30, L31, and Y93. If one or more of these RAVs is identified, then ribavirin should be added to elbasvir-grazoprevir and the treatment course extended from 12 to 16 weeks.
- For initial therapy of treatment-naïve genotype 1b patients without cirrhosis, the same 12-week regimens are used as for genotype 1a without cirrhosis, but with the following exceptions: (a) baseline 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 RAVs and (b) for treatment of genotype 1b, ribavirin is not added to the regimen ombitasvir-paritaprevir-ritonavir and dasabuvir.
- For retreatment of patients with genotype 1a who previously failed therapy with peginterferon and ribavirin, the same 12-week regimens are used as for initial treatment in genotype 1a patients without cirrhosis. For retreatment of genotype 1a patients with compensated cirrhosis, the recommended regimens are also the same as with initial treatment and compensated cirrhosis.
- For retreatment of patients with genotype 1b who previously failed therapy with peginterferon and ribavirin, the same 12-week regimens are used as for initial treatment in genotype 1b patients without cirrhosis. For retreatment of genotype 1b patients with compensated cirrhosis, the recommended regimens are: (a) elbasvir-grazoprevir, (b) ledipasvir-sofosbuvir plus ribavirin for 12 weeks, (c) ombitasvir-paritaprevir-ritonavir and dasabuvir for 12 weeks, and (d) sofosbuvir-velpatasvir for 12 weeks.
- In patients with genotype 1a or 1b infection who previously failed sofosbuvir plus ribavirin, with or without peginterferon, the recommended regimen is ledipasvir-sofosbuvir plus ribavirin; the duration of therapy is 12 weeks without cirrhosis and 24 weeks with compensated cirrhosis.
- Multiple effective options are also available for treatment-experienced patients who previously failed a regimen that included an NS3A protease inhibitor or a NS5A inhibitor.
- For treatment-naïve and treatment-experienced patients with genotype 1 infection, the new benchmark for sustained virologic response rates is 90% or greater.
- The major barrier to treatment with all new therapies is the extremely high cost of a treatment course.

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Figures

Figure 1 Estimated Cost of Medication Regimens Used to Treat Genotype 1a Chronic HCV

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

Estimated Cost* for Initial Recommend Treatment of Genotype 1a HCV	
Regimen and Duration of Therapy [^]	Cost of Regimen*
Elbasvir-Grazoprevir for 12 weeks	\$54,600
Elbasvir-Grazoprevir for 16 weeks	\$72,800
Ledipasvir-Sofosbuvir for 12 weeks	\$94,500
Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + Ribavirin for 12 weeks	\$83,819
Sofosbuvir + Simeprevir for 12 weeks	\$150,000
Sofosbuvir-Velpatasvir for 12 weeks	\$74,760
Sofosbuvir + Daclatasvir x 12 weeks	\$147,000

[^]Regimen and Duration of therapy for Initial treatment of patients with Genotype 1a without cirrhosis
^{*}Cost of regimen estimated based on Wholesale Acquisition Cost (WAC)

Figure 2 Estimated Cost of Medication Regimens Used to Treat Genotype 1b Chronic HCV

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

Estimated Cost* for Initial Recommend Treatment of Genotype 1b HCV	
Regimen and Duration of Therapy[^]	Cost of Regimen*
Elbasvir-Grazoprevir for 12 weeks	\$54,600
Ledipasvir-Sofosbuvir for 12 weeks	\$94,500
Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir for 12 weeks	\$83,319
Sofosbuvir + Simeprevir for 12 weeks	\$150,000
Sofosbuvir-Velpatasvir for 12 weeks	\$74,760
Sofosbuvir + Daclatasvir x 12 weeks	\$147,000

[^]Regimen and Duration of therapy for Initial treatment of patients with Genotype 1b without cirrhosis
^{*}Cost of regimen estimated based on Wholesale Acquisition Cost (WAC)

Genotype 1a: Initial Treatment

Table 1. Treatment-Naive Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for 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 use only if patient has NO baseline high fold-change NS5A RAVs for elbasvir detected; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

Recommended for 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 Genotype 1a patients without Cirrhosis

Ombitasvir-Pa ritaprevir- Ritonavir and Dasabuvir + **Ribavirin**

*Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75
mg)/ritonavir (50
mg) two tablets
once daily plus
dasabuvir (250 mg)
one tablet twice
daily for 12 weeks*

*1000 mg/day if <75
kg or 1200 mg/day if
≥75 kg for 12 weeks*

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

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

Recommended for Genotype 1a patients without Cirrhosis

Simeprevir + **Sofosbuvir**

150 mg once daily + 400 mg once daily

for 12 weeks

for 12 weeks

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

Recommended for 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](#)

Recommended for Genotype 1a patients without Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 12 weeks* *400 mg 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 Genotype 1a patients without Cirrhosis

**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*

For use in patients who have one or more baseline high fold-change NS5A RAVs for elbasvir; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

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

Not recommended

Recommended for Genotype 1a patients with Compensated Cirrhosis

Elbasvir- Grazoprevir

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

weeks

For use only if patient has NO baseline high fold-change NS5A RAVs for elbasvir detected; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

Recommended for Genotype 1a patients with Compensated 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 Genotype 1a 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](#)

Alternative for Genotype 1a patients with Compensated Cirrhosis

**Ombitasvir-Pa
ritaprevir-
Ritonavir and
Dasabuvir** + **Ribavirin**
1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks

**Fixed-dose combination of ombitasvir (12.5 mg)/paritaprevir (75 mg)/ritonavir (50 mg) two tablets once daily plus dasabuvir (250 mg) one tablet twice daily for 24 weeks*

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

Note: (i) *See the warning in the product information regarding risk of serious liver injury when using ombitasvir-paritaprevir-ritonavir plus dasabuvir in patients with cirrhosis, (ii) the ribavirin daily dose is given in two divided doses.

Alternative for Genotype 1a patients with Compensated Cirrhosis

Simeprevir + **Sofosbuvir**
150 mg once daily for 24 weeks + *400 mg once daily for 24 weeks*

For use only if NO Q80K polymorphism detected.

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

Alternative for Genotype 1a patients with Compensated Cirrhosis

Daclatasvir <i>60 mg* once daily for 24 weeks</i>	+	Sofosbuvir <i>400 mg once daily for 24 weeks</i>	±	Ribavirin <i>1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks</i>
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Rating: [Class IIa](#), [Level B](#)

Note: (i) *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; (ii) the ribavirin daily dose is given in two divided doses.

Alternative for Genotype 1a patients with Compensated Cirrhosis

Elbasvir- Grazoprevir <i>Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks</i>	+	Ribavirin <i>1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks</i>
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For use in patients who have one or more baseline high fold-change NS5A RAVs for elbasvir; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 1b: Initial Treatment

Table 2. Treatment-Naive Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for 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 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 Genotype 1b patients without Cirrhosis

Ombitasvir-Pa ritaprevir- Ritonavir and Dasabuvir

*Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75
mg)/ritonavir (50
mg) two tablets
once daily plus
dasabuvir (250 mg)
one tablet twice
daily for 12 weeks*

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

Recommended for Genotype 1b patients without Cirrhosis

Simeprevir + **Sofosbuvir**
*150 mg once daily 400 mg once daily
for 12 weeks for 12 weeks*

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

Recommended for 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](#)

Recommended for Genotype 1b patients without Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 12 weeks* *400 mg 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.

Recommended

Recommended for Genotype 1b patients with Compensated 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 Genotype 1b patients with Compensated 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 Genotype 1b patients with Compensated Cirrhosis

Ombitasvir-Pa ritaprevir- Ritonavir and Dasabuvir

*Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75*

mg)/ritonavir (50 mg) two tablets once daily plus dasabuvir (250 mg) one tablet twice daily for 12 weeks

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

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

Recommended for Genotype 1b 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](#)

Alternative for Genotype 1b patients with Compensated Cirrhosis

Daclatasvir	+	Sofosbuvir	±	Ribavirin
60 mg* once daily for 24 weeks		400 mg once daily for 24 weeks		1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks

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

Note: (i) *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; (ii) the ribavirin daily dose is given in two divided doses.

Alternative for Genotype 1b patients with Compensated Cirrhosis

Simeprevir	+	Sofosbuvir	±	Ribavirin
150 mg once daily for 24 weeks		400 mg once daily for 24 weeks		1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks

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

Alternative

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 1a: Retreatment

Table 3. Peginterferon plus Ribavirin Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for Retreatment of 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 use only if patient has NO baseline high fold-change NS5A RAVs for elbasvir detected; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

Recommended for Retreatment of Genotype 1a patients without Cirrhosis

Ledipasvir- Sofosbuvir

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

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

Recommended for Retreatment of Genotype 1a patients without Cirrhosis

Ombitasvir-Pa ritaprevir- Ritonavir and Dasabuvir + **Ribavirin**

*1000 mg if <75 kg
or 1200 mg if ≥75
kg for 12 weeks*

*Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75
mg)/ritonavir (50
mg) two tablets
once daily plus
dasabuvir (250 mg)
one tablet twice
daily for 12 weeks*

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

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

Recommended for Retreatment of Genotype 1a patients without Cirrhosis

Simeprevir + **Sofosbuvir**

150 mg once daily + 400 mg once daily

for 12 weeks

for 12 weeks

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

Recommended for Retreatment of 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](#)

Recommended for Retreatment of Genotype 1a patients without Cirrhosis

Daclatasvir + **Sofosbuvir**
60 mg once daily for 12 weeks* *400 mg 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 Retreatment of Genotype 1a patients without Cirrhosis

**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*

For use in patients who have one or more baseline high fold-change NS5A RAVs for elbasvir; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

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

Not recommended

Recommended for Retreatment of Genotype 1a patients with Compensated Cirrhosis

Elbasvir- Grazoprevir

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

weeks

For use only if patient has NO baseline high fold-change NS5A RAVs for elbasvir detected; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

Recommended for Retreatment of Genotype 1a patients with Compensated Cirrhosis

Ledipasvir-Sofosbuvir + **Ribavirin**
Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 12 weeks *1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks*

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

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

Recommended for Retreatment of Genotype 1a 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](#)

Alternative for Retreatment of Genotype 1a patients with Compensated Cirrhosis

Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir + **Ribavirin**
**Fixed-dose combination of ombitasvir (12.5 mg)/paritaprevir (75 mg)/ritonavir (50 mg) two tablets once daily plus dasabuvir (250 mg) one tablet twice daily for 24 weeks* *1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks*

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

Note: (i) *See the warning in the product information regarding risk of serious liver injury when using ombitasvir-paritaprevir-ritonavir plus dasabuvir in patients with cirrhosis; (ii) the ribavirin daily dose is given in two divided doses.

Alternative for Retreatment of Genotype 1a patients with Compensated Cirrhosis

Ledipasvir-Sofosbuvir
Fixed-dose combination of

ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 24 weeks

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

Alternative for Retreatment of Genotype 1a patients with Compensated Cirrhosis

<p>Elbasvir-Grazoprevir Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 16 weeks</p>	+	<p>Ribavirin 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 16 weeks</p>
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For use in patients who have one or more baseline high fold-change NS5A RAVs for elbasvir; these NS5A RAVs include genotype 1a polymorphisms at amino acid positions 28, 30, 31, or 93.

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

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

Alternative for Retreatment of Genotype 1a patients with Compensated Cirrhosis

<p>Daclatasvir 60 mg* once daily for 24 weeks</p>	+	<p>Sofosbuvir 400 mg once daily for 24 weeks</p>	±	<p>Ribavirin 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks</p>
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Rating: [Class IIa](#), [Level B](#)

Note: (i) *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; (ii) the ribavirin daily dose is given in two divided doses.

Alternative for Retreatment of Genotype 1a patients with Compensated Cirrhosis

<p>Simeprevir 150 mg once daily for 24 weeks</p>	+	<p>Sofosbuvir 400 mg once daily for 24 weeks</p>	±	<p>Ribavirin 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks</p>
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For use only if NO Q80K polymorphism is detected.

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. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 1b: Retreatment

Table 4. Peginterferon plus Ribavirin Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for Retreatment of 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 Retreatment of Genotype 1b patients without Cirrhosis

Ledipasvir- Sofosbuvir

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

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

Recommended for Retreatment of Genotype 1b patients without Cirrhosis

Ombitasvir-Pa ritaprevir- Ritonavir and Dasabuvir

*Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75
mg)/ritonavir (50
mg) two tablets
once daily plus
dasabuvir (250 mg)
one tablet twice
daily for 12 weeks*

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

Recommended for Retreatment of Genotype 1b patients without Cirrhosis

Simeprevir + **Sofosbuvir**
*150 mg once daily 400 mg once daily
for 12 weeks for 12 weeks*

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

Recommended for Retreatment of 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](#)

Recommended for Retreatment of Genotype 1b patients without Cirrhosis

Daclatasvir + Sofosbuvir

60 mg once daily
for 12 weeks* + *400 mg once daily
for 12 weeks*

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

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

Recommended

Recommended for Retreatment of Genotype 1b patients with Compensated 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 Retreatment of Genotype 1b patients with Compensated Cirrhosis

Ledipasvir- Sofosbuvir + Ribavirin

*Fixed-dose
combination of
ledipasvir (90
mg)/sofosbuvir (400
mg) once daily for
12 weeks* + *1000 mg/day if <75
kg or 1200 mg/day if
≥75 kg for 12 weeks*

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

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

Recommended for Retreatment of Genotype 1b patients with Compensated Cirrhosis

Ombitasvir-Pa ritaprevir- Ritonavir and Dasabuvir

**Fixed-dose
combination of
ombitasvir (12.5
mg)/paritaprevir (75*

mg)/ritonavir (50 mg) two tablets once daily plus dasabuvir (250 mg) one tablet twice daily for 12 weeks

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

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

Recommended for Retreatment of Genotype 1b 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](#)

Alternative for Retreatment of Genotype 1b patients with Compensated Cirrhosis

Ledipasvir-Sofosbuvir

Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 24 weeks

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

Alternative for Retreatment of Genotype 1b patients with Compensated Cirrhosis

Daclatasvir	+	Sofosbuvir	±	Ribavirin
<i>60 mg* once daily for 24 weeks</i>		<i>400 mg once daily for 24 weeks</i>		<i>1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks</i>

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

Note: (i) *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; (ii) the ribavirin daily dose is given in two divided doses.

Alternative for Retreatment of Genotype 1b patients with Compensated Cirrhosis

Simeprevir	+	Sofosbuvir	±	Ribavirin
<i>150 mg once daily for 24 weeks</i>		<i>400 mg once daily for 24 weeks</i>		<i>1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 24 weeks</i>

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. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] -

Accessed March 10, 2017.

Genotype 1: Retreatment

Table 5. Sofosbuvir plus Ribavirin, with or without Peginterferon Treatment-Experienced Patients

Recommended for Retreatment of Genotype 1a or 1b patients, without Cirrhosis

<p>Ledipasvir-Sofosbuvir Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 12 weeks</p>	+	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks</p>
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Rating: [Class IIa](#), [Level B](#)

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

Recommended

Recommended for Retreatment of Genotype 1a or 1b patients, with Compensated Cirrhosis

<p>Ledipasvir-Sofosbuvir Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 24 weeks</p>	+	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks</p>
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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. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 1: Retreatment

Table 6. HCV NS3 Protease Inhibitor (Telaprevir, Boceprevir, or Simeprevir) plus Peginterferon and Ribavirin Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended for Retreatment of Genotype 1a or 1b patients, without Cirrhosis

Ledipasvir-Sofosbuvir

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

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

Recommended for Retreatment of Genotype 1a or 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](#)

Recommended for Retreatment of Genotype 1a or 1b patients, without Cirrhosis

Daclatasvir	+	Sofosbuvir
<i>60 mg* once daily for 12 weeks</i>		<i>400 mg once daily for 12 weeks</i>

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

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

Recommended for Retreatment of Genotype 1a or 1b patients, without Cirrhosis

Elbasvir-Grazoprevir	+	Ribavirin
<i>Fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) one tablet once daily for 12 weeks</i>		<i>1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg for 12 weeks</i>

Genotype 1a patients who have one or more baseline high fold-change NS5A RAVs for elbasvir should have treatment extended to 16 weeks; these RAVs include

polymorphisms at amino acid positions 28, 30, 31, or 93.

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

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

Recommended

Recommended for Retreatment of Genotype 1a or 1b patients, with Compensated Cirrhosis

<p>Ledipasvir-Sofosbuvir Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 12 weeks</p>	+	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 12 weeks</p>
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Rating: [Class I](#), [Level A](#)

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

Recommended for Retreatment of Genotype 1a or 1b patients, with Compensated Cirrhosis

Ledipasvir-Sofosbuvir
Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) once daily for 24 weeks

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

Recommended for Retreatment of Genotype 1a or 1b 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 Retreatment of Genotype 1a or 1b patients, with Compensated Cirrhosis

<p>Daclatasvir 60 mg* once daily for 24 weeks</p>	+	<p>Sofosbuvir 400 mg once daily for 24 weeks</p>	±	<p>Ribavirin 1000 mg if <75 kg or 1200 mg if ≥75 kg for 24 weeks</p>
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Rating: [Class IIa](#), [Level B](#)

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

Recommended for Retreatment of Genotype 1a or 1b 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 if <75 kg
or 1200 mg if ≥75
kg for 12 weeks*

Genotype 1a patients who have one or more baseline high fold-change NS5A RAVs for elbasvir should have treatment extended to 16 weeks; these RAVs include polymorphisms at amino acid positions 28, 30, 31, or 93.

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. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 1: Retreatment

Table 7. Simeprevir plus Sofosbuvir Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended Retreatment of Patients with Genotype 1 and Simeprevir plus Sofosbuvir Treatment Experienced

- **Deferral of treatment is recommended, pending availability of data, for patients with HCV genotype 1 infection, regardless of subtype, in whom prior treatment with the HCV protease inhibitor simeprevir plus sofosbuvir has failed (no prior NS5A treatment), who do not have cirrhosis, and do not have reasons for urgent retreatment.**

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

- **Testing for resistance-associated variants that confer decreased susceptibility to NS3 protease inhibitors and to NS5A inhibitors is recommended for patients with HCV genotype 1 infection, regardless of subtype, in whom prior treatment with the HCV protease inhibitor simeprevir plus sofosbuvir has failed (no prior NS5A treatment), who have compensated cirrhosis or have reasons for urgent retreatment. The specific drugs used in the retreatment regimen should be tailored to the results of this testing.**

Rating: [Class II](#), [Level C](#)

- **When using nucleotide-based (eg, sofosbuvir) dual DAA therapy a treatment duration of 24 weeks is recommended, and weight-based ribavirin, unless contraindicated, should be added.**

Rating: [Class II](#), [Level C](#)

- **If available, nucleotide-based (eg, sofosbuvir) triple or quadruple DAA regimens may be considered. In these settings treatment duration ranges from 12 weeks to 24 weeks, and weight-based ribavirin, unless contraindicated, are recommended.**

Rating: [Class II](#), [Level C](#)

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

Genotype 1: Retreatment

Table 8. HCV NS5a Inhibitor Treatment-Experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

Recommended Retreatment of Patients with Genotype 1 and HCV NS5A Inhibitor Treatment Experienced

- **Deferral of treatment is recommended, pending availability of data for patients with HCV genotype 1, regardless of subtype, in whom previous treatment with any HCV nonstructural protein 5A (NS5A) inhibitors has failed, who do not have cirrhosis, and do not have reasons for urgent retreatment.**

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

- **Testing for resistance-associated variants that confer decreased susceptibility to NS3 protease inhibitors and to NS5A inhibitors is recommended for patients with HCV genotype 1, regardless of subtype, in whom previous treatment with any HCV nonstructural protein 5A (NS5A) inhibitors has failed, and who have compensated cirrhosis, or have reasons for urgent retreatment. The specific drugs used in the retreatment regimen should be tailored to the results of this testing as described below.**

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

- **When using nucleotide-based (eg, sofosbuvir) dual DAA therapy a treatment duration of 24 weeks is recommended, and weight-based RBV, unless contraindicated, should be added.**

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

- **If available, nucleotide-based (eg, sofosbuvir) triple or quadruple DAA regimens may be considered. In these settings treatment duration ranges from 12 weeks to 24 weeks, and weight-based ribavirin, unless contraindicated, are recommended.**

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

Source: AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed. [[AASLD/IDSA Hepatitis C Guidance](#)] - Accessed March 10, 2017.

