Treatment of HCV Genotype 5 or 6

Introduction

Background

In the United States, fewer than 2% of hepatitis C infections involve genotype 5 or 6 infection.[1] Genotype 5 hepatitis C infection (HCV) is endemic to South Africa where up to 40% of individuals with chronic hepatitis C from that geographic region have genotype 5 infection.[2,3] Scattered pockets of genotype 5 HCV have also been isolated from regions in Europe.[4,5] There is only one subtype of HCV genotype 5 (subtype 5a).[2] Little is known about the natural history of patients with genotype 5 HCV. Genotype 6 hepatitis C infection has been found primarily in China, Hong Kong, Korea, Taiwan, and Southeast Asia, including Thailand, Vietnam, Singapore, and Malaysia.[6,7,8] Almost all the cases of genotype 6 in the United States occur in immigrants from Asia and Southeast Asia.[9] Available data suggest that patients with genotype 6 infection have a similar natural history as those with genotype 1.[10] Because of the low prevalence of genotype 5 and 6 in clinical studies, relatively little is known about the optimal treatment of genotype 5 or 6 infection. The following discussion regarding initial treatment and retreatment of patients with genotype 5 or 6 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. The direct-acting antiviral agents exert their action at specific steps in the HCV life cycle. There are three major classes of direct-acting antiviral medications: nonstructural proteins 3/4A (NS3/4A) protease inhibitors, NS5A inhibitors, and NS5B polymerase inhibitors (Figure 1); the NS5B polymerase inhibitors include the nucleoside analogs and nonnucleoside analogs.[11,12] Adherence with the treatment regimen is extremely important. Thus, 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 5 or 6 Treatment Regimen

For patients chronically infected with genotype 5 or 6 HCV, two key factors influence the choice and duration of therapy: cirrhosis status and prior treatment experience. In addition, the cost of the regimen, insurance coverage, and patient or provider preference can play a major role in the regimen choice. For initial treatment of patients with genotype 5 or 6 HCV infection, the estimated wholesale acquisition cost for regimens in the recommended category in the American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD-IDSA) guidance ranges from approximately $26,400 for those without cirrhosis to $94,500 for those with compensated cirrhosis (Figure 2). The following treatment recommendations are based on the
AASLD-IDSA hepatitis C treatment guidance for patients with genotype 5 or 6 HCV.[13,14]

- AASLD-IDSA HCV Guidance for Treatment-Naïve Patients with Genotype 5 or 6 HCV
- AASLD-IDSA HCV Guidance for Treatment-Experienced Patients with Genotype 5 or 6 HCV
HCV Genotype 5 or 6: Initial Treatment

Background

There are relatively few dedicated studies related to the treatment of patients with genotype 5 or 6 chronic HCV infection, particularly for direct-acting antiviral agents. Older studies in treatment-naïve patients with genotype 5 infection that have examined the combination of interferon (either standard or pegylated) with ribavirin for 48 weeks have reported sustained virologic response rates at 12 weeks post-treatment (SVR12) of approximately 55 to 70%. Most studies that have addressed initial treatment of patients with genotype 6 are observational and with small sample sizes, reporting sustained virologic response rates of 70 to 80% with peginterferon plus ribavirin when given for 48 weeks (and only slightly lower when given for 24 weeks). Available data suggest SVR12 rates can be greater than 95% with glecaprevir-pibrentasvir, sofosbuvir-velpatasvir, or ledipasvir-sofosbuvir for the initial therapy of genotype 5 or 6.

Factors to Consider Prior to Choosing Treatment Regimen

For patients chronically infected with genotype 5 or 6 hepatitis C, little is known regarding baseline factors that may predict response to therapy, but as with other genotypes, cirrhosis and treatment experience probably play a role. The management of genotype 5 or 6 patients with decompensated cirrhosis, renal impairment, HIV coinfection, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD-IDSA HCV Guidance for Initial Treatment of HCV Genotype 5 and 6

The following is a summary of AASLD-IDSA HCV Guidance for initial treatment patients with hepatitis C genotype 5 or 6 infection, including those without cirrhosis and those with compensated cirrhosis. 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 5 or 6: Initial Treatment

<table>
<thead>
<tr>
<th>Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glecaprevir-Pibrentasvir</strong></td>
</tr>
<tr>
<td>*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks</td>
</tr>
<tr>
<td>For patients without cirrhosis</td>
</tr>
<tr>
<td>Rating: <strong>Class I, Level A</strong></td>
</tr>
<tr>
<td>Note: *This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).</td>
</tr>
</tbody>
</table>

Recommended regimens listed by evidence level and alphabetically

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**Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis**

**Glecaprevir-Pibrentasvir**

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

For patients without cirrhosis

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

For patients with compensated cirrhosis

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 5 or 6 Patients With and Without Compensated Cirrhosis**

**Glecaprevir-Pibrentasvir**

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

For patients with and without compensated cirrhosis

Rating: **Class I, Level A**

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**Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis**

**Sofosbuvir-Velpatasvir**

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

For patients with and without compensated cirrhosis

Rating: **Class I, Level B**

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**Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis**

**Ledipasvir-Sofosbuvir**

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

For patients with and without compensated cirrhosis

Rating: **Class IIa, Level B**

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


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**Key Studies for Initial Treatment of Patients with Genotype 5 or 6**

The following key studies support the recommendations for treatment of patients with chronic hepatitis C and genotype 5 or 6 infection who are treatment naïve.

**Glecaprevir-Pibrentasvir**

- **SURVEYOR-I and SURVEYOR-II**: The SURVEYOR-I (genotypes 1, 4, 5 and 6) and SURVEYOR-II (genotypes 2 and 3) were phase 2 open-label trials of treatment-naïve and treatment-experienced adults without cirrhosis.[29] In the SURVEYOR-I trial, participants with HCV genotype 4, 5, or 6 received 12 weeks of glecaprevir-pibrentasvir. Among those enrolled and treated, one had HCV genotype 5 and 11 had HCV genotype 6. For the participants with HCV genotype 5 or 6, 100% (12 of 12) achieved an SVR12 (data not provided for number of treatment-naïve versus treatment-experienced patients with HCV genotype 5 or 6).
- **EXPEDITION-1**: This phase 3, single-arm, open-label trial evaluated the safety and efficacy of 12 weeks of glecaprevir-pibrentasvir in treatment-naïve and treatment-experienced adults with compensated cirrhosis and HCV genotype 1, 2, 4, 5, or 6 infection.[25] All (100%) of
patients with genotype 5 (n=2) or genotype 6 (n=7) achieved an SVR12.

Ledipasvir-Sofosbuvir

- **New Zealand Genotype 3 and 6 Study**: In this open-label, phase 2 study performed at two centers in New Zealand, investigators enrolled treatment-naïve and treatment-experienced adults with HCV genotype 3 or 6 infection. One arm of this study enrolled 25 participants with HCV genotype 6 to receive a 12-week course of ledipasvir-sofosbuvir. Overall, 96% (24 of 25) individuals with HCV genotype 6 achieved an SVR12; the one person in this cohort who did not achieve an SRV12 withdrew from the study at week 8. Only two of the treatment-naïve individuals with genotype 6 had cirrhosis.

- **Ledipasvir-Sofosbuvir for Genotype 5 Infection**: In a phase 2, open-label study conducted in France, investigators enrolled 21 treatment-naïve and 20 treatment-experienced adults with HCV genotype 5 infection to receive a 12-week course of ledipasvir-sofosbuvir. For the treatment-naïve individuals with HCV genotype 5 infection, 95% (20 of 21) achieved an SVR12. The results for participants with genotype 5 infection were similar regardless of cirrhosis status.

Sofosbuvir-Velpatasvir

- **ASTRAL-1**: In the phase 3 ASTRAL-1 trial, investigators randomized treatment-naïve and treatment-experienced adults with chronic hepatitis C genotype 1, 2, 4, 5, or 6 infection in a 5:1 ratio to receive a 12-week course of either sofosbuvir-velpatasvir or placebo. The study included 34 patients with HCV genotype 5 infection and 41 with genotype 6. Among the treatment-naïve participants treated with sofosbuvir-velpatasvir, 96% (23 of 24) with genotype 5 infection achieved an SVR12 and 100% (38 of 38) with genotype 6 achieved an SVR12.

- **POLARIS-2**: In this phase 3, open-labeled trial, 94% (17 of 18) patients with genotype 5 who received 8 weeks of sofosbuvir-velpatasvir-voxilaprevir achieved an SVR12. All 30 patients with genotype 6 who received 8 weeks of sofosbuvir-velpatasvir-voxilaprevir and all 9 patients with genotype 6 who received a 12-week course of sofosbuvir-velpatasvir achieved an SVR12.
HCV Genotype 5 or 6: Retreating Persons who Failed Prior Therapy

Background

Given the very low prevalence of genotypes 5 and 6 in settings where HCV therapy is accessible, limited data and experience exist with retreatment of patients with genotype 5 or 6. Recommendations are primarily based on available data in small numbers of treatment-experienced individuals with genotype 5 or 6 from clinical studies, and by extrapolating from experience with other HCV genotypes.

Factors to Consider Prior to Choosing Treatment Regimen

For patients chronically infected with genotype 5 or 6 hepatitis C, insufficient data exist regarding the impact of cirrhosis on the optimal retreatment regimen or duration of therapy given the small numbers of patients in these trials. The retreatment of genotype 5 or 6 patients with decompensated cirrhosis, renal impairment, HIV coinfection, acute hepatitis C infection, or post-liver transplantation is not addressed in this lesson.

AASLD-IDSA HCV Guidance for Retreatment of HCV Genotype 5 or 6

The following is a summary of AASLD-IDSA HCV Guidance for retreatment of adults with hepatitis C genotype 5 or 6 infection, including those without cirrhosis and those with compensated cirrhosis.[30,31] 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 2. AASLD-IDSA HCV Guidance for Genotype 5 or 6: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

| Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis
|---|
| **Glecaprevir-Pibrentasvir**  
*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*  
for patients without cirrhosis

Rating: **Class Ia, 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 Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis
|---|
| **Glecaprevir-Pibrentasvir**  
*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*  
for patients with compensated cirrhosis

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).*
mg)/pibrentasvir (40 mg).

**Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients**

<table>
<thead>
<tr>
<th>Ledipasvir-Sofosbuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks</td>
</tr>
</tbody>
</table>

for patients with or without compensated cirrhosis

Rating: **Class IIa, Level B**

**Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients**

<table>
<thead>
<tr>
<th>Sofosbuvir-Velpatasvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks</td>
</tr>
</tbody>
</table>

for patients with or without compensated cirrhosis

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. Retreatment of persons in whom prior therapy has failed: peginterferon plus ribavirin-experienced, genotype 5 or 6 patients with or without compensated cirrhosis [AASLD-IDSA Hepatitis C Guidance] - Accessed November 24, 2017.

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**Table 3. AASLD-IDSA HCV Guidance for Genotype 5 or 6: Retreatment DAA-Experienced (Including NS5A Inhibitors), Genotype 5 or 6 Patients**

<table>
<thead>
<tr>
<th>Sofosbuvir-Velpatasvir-Voxilaprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks</td>
</tr>
</tbody>
</table>

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. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A inhibitors), genotype 5 or 6 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance] - Accessed November 15, 2017.
Key Studies for Retreatment of Adults with HCV Genotype 5 or 6

There are limited data from studies that adequately address the retreatment of adults with HCV genotype 5 or 6 infection who failed prior therapy.

Glecaprevir-Pibrentasvir

- **SURVEYOR-I and SURVEYOR-II**: The SURVEYOR-I (genotypes 1, 4, 5 and 6) and SURVEYOR-II (genotypes 2 and 3) were phase 2 open-label trials of treatment-naïve and treatment patients without cirrhosis who were treatment naïve or treatment experienced.[29] In the SURVEYOR-I trial, patients with genotype 4, 5, or 6 received 12 weeks of glecaprevir-pibrentasvir. Among those enrolled and treated, one had genotype 5 and 11 had genotype 6. All patients (100%) with genotype 5 or 6 achieved an SVR12 (data not provided for number of treatment-naïve versus treatment-experienced patients with genotype 5 or 6).

- **EXPEDITION-1**: In this phase 3 single-arm open-label trial evaluated the safety and efficacy of 12 weeks of glecaprevir-pibrentasvir in treatment-naive and treatment-experienced adults with compensated cirrhosis and genotype 1, 2, 4, 5, or 6 hepatitis C infection.[25] All (100%) of patients with genotype 5 (n=2) or genotype 6 (n=7) achieved an SVR12 (data not provided for number of treatment-naïve versus treatment-experienced patients with genotype 5 or 6).

Ledipasvir-Sofosbuvir

- **Ledipasvir-Sofosbuvir for Genotype 5 Infection**: In a small, open-label study conducted in France, investigators enrolled 21 treatment-naive and 20 treatment experienced patients with HCV genotype 5 infection to receive a 12-week course of ledipasvir-sofosbuvir.[27] For the treatment-experienced patients with genotype 5 infection, 19 (95%) of 20 achieved an SVR12. The results in patients with genotype 5 were similar regardless of cirrhosis status.

Sofosbuvir-Velpatasvir

- **ASTRAL-1**: In the phase 3 ASTRAL-1 trial, investigators randomized treatment-naive and treatment-experienced patients with chronic hepatitis C genotype 1, 2, 4, 5, or 6 infection in a 5:1 ratio to receive a 12-week course of sofosbuvir-velpatasvir or placebo.[26] The study included 34 patients with genotype 5 and 41 with genotype 6. Among the treatment-experienced patients treated with sofosbuvir-velpatasvir, 11 (100%) of 11 with genotype 5 infection achieved an SVR12 and 3 (100%) of 3 with genotype 6 achieved an SVR12.

Sofosbuvir-Velpatasvir-Voxilaprevir

- **POLARIS-1**: In this phase 3 placebo-controlled trial, investigators enrolled patients with chronic hepatitis C genotype 1-6 who had previously received treatment that included an NS5A inhibitor to receive sofosbuvir-valpatasvir-voxilaprevir for 12 weeks.[32] Patients with genotype 2-6 were all assigned to the active arm. Most patients were either ledipasvir- or daclatasvir-experienced (51% and 27% respectively) and compensated cirrhosis was present in 46% of patients in the active arm. For the patients with genotype 5 (n=1) or genotype 6 infection (n= 6), all (100%) achieved an SRV12.
Summary Points

- Genotype 5 hepatitis C virus infection is uncommon in the United States, but endemic in South Africa.
- Genotype 6 hepatitis C virus infection is also infrequently seen in the United States and primarily is found in China, Korea, Taiwan, and Southeast Asia.
- Recommendations for initial treatment or retreatment are based on in vitro data and limited data from clinical trials.
- The recommended regimens for initial treatment or retreatment of patients with genotype 5 or 6 include: glecaprevir-pibrentasvir (8 weeks in patients without cirrhosis, 12 weeks in those with cirrhosis), sofosbuvir-velpatasvir (12 weeks), or ledipasvir-sofosbuvir (12 weeks).
- The recommended regimens for retreatment of peginterferon plus ribavirin-experienced genotype 5 or 6 patients are the same as for initial treatment: glecaprevir-pibrentasvir (8 or 12 weeks depending on cirrhosis status), ledipasvir-sofosbuvir, or sofosbuvir-velpatasvir.
- The recommended regimen for retreatment of DAA-experienced (including NS5A inhibitors) genotype 5 or 6 is sofosbuvir-velpatasvir-voxilaprevir.
Citations


13. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C.
Treatment-Naive Genotype 5 or 6.
[AASLD-IDSA Hepatitis C Guidance] -

14. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C.
Treatment-Experienced Genotype 5 or 6.
[AASLD-IDSA Hepatitis C Guidance] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -


28. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Initial treatment of HCV infection: treatment-naive genotype 5 or 6. [AASLD-IDSA Hepatitis C Guidance]


30. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: peginterferon plus ribavirin-experienced, genotype 5 or 6 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance]

31. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Retreatment of persons in whom prior therapy has failed: DAA-experienced (including NS5A inhibitors), genotype 5 or 6 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance]


References

- European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C 2015. [EASL]


## Figures

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

<table>
<thead>
<tr>
<th>NS3/4A Protease Inhibitors</th>
<th>NS5A Inhibitors</th>
<th>NS5B Polymerase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boceprevir</td>
<td>Daclatasvir</td>
<td>Dasabuvir</td>
</tr>
<tr>
<td>Glecaprevir</td>
<td>Elbasvir</td>
<td>Sofosbuvir</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>Ledipasvir</td>
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<tr>
<td>Paritaprevir</td>
<td>Ombitasvir</td>
<td></td>
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<tr>
<td>Simeprevir</td>
<td>Pibrentasvir</td>
<td></td>
</tr>
<tr>
<td>Telaprevir</td>
<td>Velpatasvir</td>
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<tr>
<td>Voxilaprevir</td>
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</tbody>
</table>
**Figure 2 Cost of Medication Regimens Used to Treat Genotypes 5 or 6 Chronic HCV**

This figure shows the approximate cost of a treatment course with AASLD-IDSA recommended regimens for treatment-naive patients with genotype 5 or 6 chronic HCV, including those without cirrhosis and those with compensated cirrhosis. The cost listed is based on available wholesale acquisition price data.

<table>
<thead>
<tr>
<th>Regimens and Duration of Therapy</th>
<th>Cost of Regimen*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glecaprevir-Pibrentasvir for 8 weeks</td>
<td>$26,400</td>
</tr>
<tr>
<td>Glecaprevir-Pibrentasvir for 12 weeks</td>
<td>$39,600</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir for 12 weeks</td>
<td>$74,760</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir for 12 weeks</td>
<td>$94,500</td>
</tr>
</tbody>
</table>

*Cost estimates based on Wholesale Acquisition Cost (WAC)
# Table 1. AASLD-IDSA HCV Guidance for Genotype 5 or 6: Initial Treatment

## Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis

Recommended regimens listed by evidence level and alphabetically

| Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis | Glecaprevir-Pibrentasvir | Rating: **Class I, Level A**  
*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks*  
For patients without cirrhosis |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

| Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis | Glecaprevir-Pibrentasvir | Rating: **Class I, Level A**  
*Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 12 weeks*  
For patients with compensated cirrhosis |
<table>
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<td></td>
</tr>
</tbody>
</table>

| Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis | Sofosbuvir-Velpatasvir | Rating: **Class I, Level B**  
*Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks*  
For patients with and without compensated cirrhosis |
| --- | --- | --- |

| Recommended for Treatment-Naïve Genotype 5 or 6 Patients With and Without Compensated Cirrhosis | Ledipasvir-Sofosbuvir | Rating: **Class Ia, Level B**  
*Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) one tablet once daily for 12 weeks*  
For patients with and without compensated cirrhosis |
| --- | --- | --- |

^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
### Table 2. AASLD-IDSA HCV Guidance for Genotype 5 or 6: Retreatment Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically

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<tr>
<th>Recommended for Peginterferon plus Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glecaprevir-Pibrentasvir</strong></td>
</tr>
<tr>
<td><em>Fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) once daily for 8 weeks for patients without cirrhosis</em></td>
</tr>
<tr>
<td>Rating: Class IIa, Level B</td>
</tr>
<tr>
<td>Note: <em>This is taken as 3 tablets once daily with each fixed-dose tablet containing glecaprevir (100 mg)/pibrentasvir (40 mg).</em></td>
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<td>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) one tablet once daily for 12 weeks for patients with or without compensated cirrhosis</td>
</tr>
<tr>
<td>Rating: Class IIa, Level B</td>
</tr>
</tbody>
</table>

^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 plus ribavirin-experienced, genotype 5 or 6 patients with or without compensated cirrhosis [AASLD-IDSA Hepatitis C Guidance] - Accessed November 24, 2017.
Table 3. AASLD-IDSA HCV Guidance for Genotype 5 or 6: Retreatment DAA-Experienced (Including NS5A Inhibitors), Genotype 5 or 6 Patients With or Without Compensated Cirrhosis^  

<table>
<thead>
<tr>
<th>Recommended for DAA-Experienced (Including NS5A Inhibitors), Genotype 5 or 6 Patients With or Without Compensated Cirrhosis^</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sofosbuvir-Velpatasvir-Voxilaprevir</strong></td>
<td></td>
</tr>
<tr>
<td>Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) one tablet once daily for 12 weeks</td>
<td></td>
</tr>
<tr>
<td>Rating: <strong>Class IIA, Level B</strong></td>
<td></td>
</tr>
</tbody>
</table>

^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: DAA-experienced (including NS5A inhibitors), genotype 5 or 6 patients with or without compensated cirrhosis. [AASLD-IDSA Hepatitis C Guidance] - Accessed November 15, 2017.