IMPORTANT REMINDER
This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description
Ledipasvir-sofosbuvir (Harvoni) is an oral direct-acting antiviral combination medication used for the treatment of chronic genotype 1, 4, 5, and 6 hepatitis C virus (HCV) infection.
Policy/Criteria

I. Most contracts require prior authorization approval of ledipasvir-sofosbuvir (Harvoni) prior to coverage. Ledipasvir-sofosbuvir (Harvoni) may be considered medically necessary when criteria A through D below are met.

A. There is a diagnosis of chronic genotype 1, 4, 5, or 6 hepatitis C virus (HCV) infection.

AND

B. Documentation of pre-treatment HCV RNA is provided.

AND

C. Ledipasvir-sofosbuvir (Harvoni) will be used in combination with ribavirin if used in the following treatment groups:
   1. Post-liver transplant
   OR
   2. Decompensated cirrhosis (Child-Pugh B or C)
   OR
   3. HCV genotype 1 treatment-experienced patients with compensated cirrhosis (Child-Pugh A)

AND

D. Cycle Management Program requirements are met [refer to OmedaRx Medication Policy Manual, Cycle Management Program, dru404].

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers ledipasvir-sofosbuvir (Harvoni) to be a self-administered medication.

B. When prior authorization is approved, ledipasvir-sofosbuvir (Harvoni) may be authorized in quantities up to #28 ledipasvir 90 mg-sofosbuvir 400 mg tablets per 28 days as follows:

   1. HCV genotype 1:
      a. Pre-treatment HCV RNA less than 6 million IU/mL, treatment-naive, without cirrhosis: **8 weeks total (one treatment course)**
      b. Treatment-experienced members with compensated cirrhosis (Child-Pugh A) when there is documentation that ribavirin is contraindicated or not tolerated: **24 weeks total (one treatment course)**
      c. All other patients with HCV genotype 1: **12 weeks total (one treatment course)**

   2. HCV Genotype 4, 5, or 6; treatment-naive and treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A): 12 weeks total (one treatment course)

   3. Prior liver transplant: 12 weeks total (one treatment course)
III. Ledipasvir-sofosbuvir (Harvoni) is considered investigational when used:
A. As retreatment when there has been relapse after, or no response to, a prior treatment course with a direct-acting antiviral for HCV [except boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek)] (see Appendix 1).
B. In combination with any other direct-acting antiviral for HCV (see Appendix 1).
C. Perioperatively to prevent HCV reinfection in patients receiving a liver transplant.
D. When used for the treatment of HCV genotypes other than genotype 1, 4, 5, or 6.

Position Statement
- Ledipasvir-sofosbuvir (Harvoni) is an oral combination hepatitis C virus (HCV) NS5A inhibitor (ledipasvir) and HCV polymerase inhibitor (sofosbuvir) that is used for the treatment of adult with chronic genotype 1, 4, 5, or 6 HCV infection.
- The primary endpoint evaluated in most HCV clinical trials is rate of viral cure, defined as a sustained virologic response (SVR) 12 weeks following the completion of therapy. Although SVR is considered a surrogate endpoint, it is accepted as a measure of efficacy for the treatment of HCV.
- Ledipasvir-sofosbuvir (Harvoni) has been shown to be safe and effective for treating chronic HCV infection in treatment-naïve patients, as well as in patients who relapsed after or did not respond to prior treatment with peginterferon and ribavirin or a protease inhibitor-based [e.g. boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek)] triple therapy regimen.
- Ledipasvir-sofosbuvir (Harvoni) has not been adequately studied in patients who have failed a prior sofosbuvir-based regimen. While guidelines recommend ledipasvir-sofosbuvir (Harvoni) for patients who have failed a sofosbuvir-based regimen, the recommendations are based on small pilot studies and expert opinion only. There is currently no published, phase III data supporting the efficacy of ledipasvir-sofosbuvir (Harvoni) in patients who have failed prior therapy with a sofosbuvir-containing regimen. Additional studies are needed to identify the optimal regimen and duration.
- The safety and efficacy of ledipasvir-sofosbuvir (Harvoni) in combination with other direct-acting antivirals (see Appendix 1) have not been established.
- The duration of treatment with ledipasvir-sofosbuvir (Harvoni) is based on treatment history and presence or absence of cirrhosis.
- The duration of therapy for most patients is 8 to 12 weeks and the addition of ribavirin is required in certain high-risk patients.
- The prescribing information lists 24 weeks of therapy as an option for treatment-experienced patients with HCV genotype 1 and cirrhosis; however, 12-weeks of sofosbuvir-ledipasvir (Harvoni) in combination with ribavirin produces similar rates of SVR, thus it provides a better value for members. Twenty-four weeks of therapy may be considered in treatment-experienced cirrhotics with HCV genotype who have a documented intolerance or to contraindication to ribavirin.
In treatment naïve, non-cirrhotic patients with HCV genotype and a pre-treatment HCV RNA of less than 6 million IU/mL, eight weeks of treatment has been shown to be safe and effective. In clinical trials, rates of SVR were comparable to patients who received 12 weeks of therapy in this population.

Ledipasvir-sofosbuvir (Harvoni) in combination with ribavirin has been evaluated in liver transplant recipients and patients with decompensated cirrhosis. Reported treatment success rates in patients with decompensated cirrhosis (Child-Pugh B or C) ranged from 87-88%. Rates of SVR in post-transplant patients were generally high (greater than or equal to 89%); however the rate of SVR was lower (57%, 4/7 patients) in patients with Child-Pugh C decompensated cirrhosis. Rates of SVR were similar regardless of whether patients received 12 or 24 weeks of therapy.

Ledipasvir-sofosbuvir (Harvoni) is currently being studied in a variety of HCV clinical settings. While there is limited evidence in several non-FDA approved settings, the evidence is considered preliminary and investigational.

Clinical Efficacy

HCV Genotype 1: Treatment-Naïve Patients

Ledipasvir-sofosbuvir (Harvoni) has been shown to produce high viral cure rates in treatment-naïve patients with chronic genotype 1 hepatitis C virus (HCV) infection.

- Two published trials (ION-1 and ION-3) evaluated ledipasvir-sofosbuvir in treatment-naïve patients. [1,2] ION-1 included cirrhotic patients, whereas ION-3 did not.
- In ION-1, patients were treated with ledipasvir-sofosbuvir (Harvoni) for 12 or 24 weeks with or without ribavirin. [1] In ION-3, patients were treated with ledipasvir-sofosbuvir (Harvoni) for 8 weeks with or without ribavirin, or with ledipasvir-sofosbuvir (Harvoni) without ribavirin for 12 weeks. [2]
- Both trials included a fair number of historically difficult to treat patients including those with a non-CC IL28B genotype (70-73%), black patients (12-19%), and those with HCV genotype 1a (67-80%). In ION-1, 16% of patients had cirrhosis of the liver. The following overall SVR rates were reported in ION-1 and ION-3:

<table>
<thead>
<tr>
<th></th>
<th>8 weeks</th>
<th>12 weeks</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>ledipasvir-sofosbuvir</td>
<td>94%</td>
<td>95-99%</td>
<td>98%</td>
</tr>
<tr>
<td>ledipasvir-sofosbuvir + ribavirin</td>
<td>93%</td>
<td>97%</td>
<td>99%</td>
</tr>
</tbody>
</table>

* In ION-3, among treatment-naïve, non-cirrhotic patients with a baseline HCV RNA less than 6 million IU per mL, the SVR12 was 97% (119/123) with 8-weeks of treatment versus 96% (126/131) with 12-weeks of treatment.
* In both studies, SVR rates were not significantly different between groups regardless of concomitant ribavirin therapy, cirrhosis status, or HCV genotype 1 subtype (1a vs 1b). [1,2]
* Less than 1% of patients in ION-1 and ION-3 had virologic breakthrough (on-treatment failure).
* Relapse occurred in < 1% of ION-1 study patients and in 4% of ION-3 patients. Among patients who relapsed in ION-3, the majority (87%) received 8 weeks of therapy vs 12 weeks of therapy. [1,2]
HCV Genotype 1: Treatment-Experienced Patients

Ledipasvir-sofosbuvir (Harvoni) has been shown to produce high viral cure rates in treatment-experienced patients with chronic genotype 1 HCV infection.

- The ION-2 study evaluated ledipasvir-sofosbuvir (Harvoni) in treatment experienced patients, including prior relapers, partial responders, and null responders. [3]
- Patients were treated with ledipasvir-sofosbuvir (Harvoni) for 12 or 24 weeks with or without ribavirin. [3]
- ION-2 included a fair number of historically difficult to treat patients including those with a non-CC IL28B genotype (88%), cirrhotics (20%), black patients (14-22%), and those with HCV genotype 1a (78-79%).
- The following overall SVR rates were reported in ION-2:

<table>
<thead>
<tr>
<th>Regimen</th>
<th>12 weeks</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>ledipasvir-sofosbuvir</td>
<td>94%</td>
<td>99%</td>
</tr>
<tr>
<td>ledipasvir-sofosbuvir + ribavirin</td>
<td>96%</td>
<td>99%</td>
</tr>
</tbody>
</table>

* SVR rates were not significantly different between groups regardless of concomitant ribavirin therapy, HCV genotype 1 subtype (1a vs 1b), prior treatment response (relapse vs non-response), and prior treatment history (peginterferon and ribavirin vs protease inhibitor-based triple therapy). [3]
* Significantly more patients with cirrhosis who were treated for 24 weeks achieved SVR as compared to those who were treated for 12 weeks (100% vs 82-86%, respectively; P = 0.007). [3]
* Less than 1% of patients in ION-2 had virologic breakthrough (on-treatment failure). [3]
* Relapse occurred in 2.5% of ION-2 study patients, all of whom were treated for 12 weeks. [3]

- The SIRIUS study evaluated patients with HCV genotype 1 and compensated cirrhosis who had not achieved SVR after successive treatments with pegylated interferon and protease-inhibitor regimens. [4] Patients were randomly assigned to received ledipasvir-sofosbuvir (Harvoni) plus ribavirin for 12 weeks or ledipasvir-sofosbuvir (Harvoni) for 24 weeks. In total, 77 patients were randomized to each treatment group. The following overall SVR rates were reported in SIRIUS:

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ledipasvir-sofosbuvir</td>
<td>24 weeks</td>
<td>96%</td>
</tr>
<tr>
<td>ledipasvir-sofosbuvir + ribavirin</td>
<td>12 weeks</td>
<td>97%</td>
</tr>
</tbody>
</table>

HCV Genotype 4

Ledipasvir-sofosbuvir (Harvoni) has been shown to produce high viral cure rates in treatment-experienced patients with chronic genotype 4 HCV infection. [5]

- Study 1119 evaluated treatment-naive and treatment-experienced patients with HCV genotype 4, including patients with cirrhosis. All patients received sofosbuvir-ledipasvir (Harvoni) for 12 weeks. The overall SVR12 rate was 93% (41/44). Rates of SVR were similar regardless of prior HCV treatment history and cirrhosis status.
The ION-4 study included HCV/HIV coinfected patients with HCV genotype 1 or 4. Although the study only included eight patients with HCV Genotype 4, all achieved an SVR.

HCV Genotypes 5 and 6
Ledipasvir-sofosbuvir (Harvoni) has been shown to produce high viral cure rates in treatment-experienced patients with chronic genotype 5 or 6 HCV infection.

- Study 1119 evaluated treatment-naive or previously-treated subjects with HCV genotype 5, with or without cirrhosis. All patients received sofosbuvir-ledipasvir (Harvoni) for 12 weeks. The overall SVR12 was 93% (38/41). Rates of SVR12 were similar regardless of prior HCV treatment history and cirrhosis status. [5]
- The ELECTRON-2 trial evaluated treatment-naive or treatment-experienced patients with HCV genotype 6, with or without cirrhosis. The overall SVR12 was 96% (24/25). Rates of SVR12 were similar regardless of prior HCV treatment history and cirrhosis status. [5]

HCV/HIV Coinfection
Ledipasvir-sofosbuvir (Harvoni) has been shown to produce high viral cure rates in patients with HCV/HIV coinfection.

- ION-4 evaluated ledipasvir-sofosbuvir (Harvoni), without ribavirin, for 12 weeks in 335 patients with HCV/HIV coinfection. SVR rates were similarly high between all treatment groups (96-100%) and rates were consistently high regardless of genotype, prior treatment history (dual therapy or triple therapy), and presence or absence of cirrhosis. [6]
- The following overall SVR rates were reported in ION-4:

<table>
<thead>
<tr>
<th>Population</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a</td>
<td>96% (240/250)</td>
</tr>
<tr>
<td>Genotype 1b</td>
<td>96% (74/77)</td>
</tr>
<tr>
<td>Genotype 4</td>
<td>100% (8/8)</td>
</tr>
</tbody>
</table>

Post-Transplant
Ledipasvir-sofosbuvir (Harvoni) in combination with ribavirin has been shown to produce high viral cure rates in patients who have previously received a liver transplant.

- The SOLAR-1 and SOLAR-2 studies evaluated ledipasvir-sofosbuvir (Harvoni) plus ribavirin for 12 or 24 weeks in patients who had received a liver transplant or who had decompensated cirrhosis (Child-Pugh B or C). Rates of SVR were similar in patients who received 12 or 24 weeks of therapy. Rates of SVR in patients who received 12 weeks of therapy are shown in the following table:
<table>
<thead>
<tr>
<th>Population</th>
<th>SVR12 (N = 300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant</td>
<td></td>
</tr>
<tr>
<td>CPT B</td>
<td>87% (45/22)</td>
</tr>
<tr>
<td>CPT C</td>
<td>88% (35/40)</td>
</tr>
<tr>
<td>Post-transplant</td>
<td></td>
</tr>
<tr>
<td>Metavir F0-F3</td>
<td>95% (94/99)</td>
</tr>
<tr>
<td>CPT A</td>
<td>98% (55/56)</td>
</tr>
<tr>
<td>CPT B</td>
<td>89% (41/46)</td>
</tr>
<tr>
<td>CPT C</td>
<td>57% (4/7)</td>
</tr>
</tbody>
</table>

CPT = Child-Pugh-Turcotte

- For patients with HCV genotype 1 or 4 with decompensated cirrhosis, guidelines recommend ledipasvir-sofosbuvir (Harvoni) with ribavirin for 12 weeks, sofosbuvir-velpatasvir (Epclusa) with ribavirin for 12 weeks, or daclatasvir (Daklinza) plus sofosbuvir (Sovaldi) with ribavirin for 12 weeks.

**Not Medically Necessary and Investigational Uses**

- The safety and efficacy of ledipasvir-sofosbuvir (Harvoni) in combination with other treatments for chronic HCV infection have not been established.
- The safety and efficacy of ledipasvir-sofosbuvir (Harvoni) has not been established in patients previously treated with a sofosbuvir-containing regimen. [7]
  * Although small pilot studies have evaluated retreatment with ledipasvir-sofosbuvir (Harvoni) in patients who failed a previous sofosbuvir-containing regimen, data from larger well designed trials are needed to establish efficacy in this setting.
  * The AASLD/IDSA treatment guidelines acknowledge that clinical trial experience and clinical trial data in this retreatment setting is very limited.
- One small, open-label phase II trial evaluated a 4-week perioperative course of ledipasvir-sofosbuvir (Harvoni) in patients receiving a liver transplant. Although the results were promising, further studies are needed to establish the safety and efficacy of ledipasvir-sofosbuvir (Harvoni) in this setting. [8]

**Effect of Baseline HCV Polymorphisms on Treatment Response**

- The presence of HCV polymorphisms have been associated with lower SVR rates in specific HCV settings [e.g. patients with baseline NS5A polymorphisms had reduced rates of SVR with a 12-week elbasvir-grazoprevir (Zepatier) regimen]. However, routine testing for resistance-associated variants (RAVs) is not recommended except for patients starting elbasvir-grazoprevir (Zepatier) or simeprevir (Olysio) plus sofosbuvir (Sovaldi). [7]
- In ION-1 and ION-3, treatment-naïve subjects with HCV genotype 1 who had baseline NS5A polymorphisms at resistance-associated positions (amino acid positions 24, 28, 30, 31, 58, 92, or 93) had relapse rates of 6% (3/48) after 8 weeks and 1% (1/113) after 12 weeks of treatment with ledipasvir-sofosbuvir (Harvoni). This was comparable to relapse rates among subjects without baseline NS5A polymorphisms: 5% (8/167) after 8 weeks and 1% (3/306) after 12 weeks. [5]
- In ION-2, treatment-experienced subjects with HCV genotype 1 who had baseline NS5A polymorphisms had relapse rates of 22% (5/23) after 12 weeks and 0% (0/19) after 24 weeks of treatment with ledipasvir-sofosbuvir (Harvoni). [5]

- In SIRIUS, treatment-experienced subjects with HCV genotype 1 who had baseline NS5A polymorphisms had a relapse rate of 0% (0/15) after 12 weeks of ledipasvir-sofosbuvir (Harvoni) plus ribavirin compared to a relapse rate of 13% (2/15) after 24 weeks of ledipasvir-sofosbuvir (Harvoni) alone. [5]

- The NS5B S282T substitution associated with resistance to sofosbuvir was not detected in the baseline NS5B sequence of any subject in Phase 3 trials by population or deep nucleotide sequence analysis. [5]

  * SVR was achieved in all 24 subjects (N=20 with L159F+C316N; N=1 with L159F; and N=3 with N142T) who had baseline polymorphisms associated with resistance to sofosbuvir and/or other NS5B nucleoside inhibitors.

- Low virologic failure rates were observed in Study 1119 and ELECTRON-2. Although the data is limited, baseline HCV NS5A resistance-associated polymorphisms are not expected to reduce the rate of SVR when ledipasvir-sofosbuvir (Harvoni) is used as recommended to treat patients with HCV genotype 4, 5, or 6 infections. [5]

  * The specific baseline polymorphisms observed in subjects with virologic failure were L28M/V, L30R, and P58T for genotype 4; L31M for genotype 5; and Q24K, F28V, R30A and T58P for genotype 6.
**Clinical Guidelines**[7]

As of October 2016, the Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) clinical guidelines recommend the following regimens for treatment-naïve patients with HCV.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Recommended Regimens</th>
<th>Alternative Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment-naïve patients</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 1a Without Cirrhosis | Elbasvir-grazoprevir x 12 weeks (if no baseline NS5A RAVs)  
Ledipasvir-sofosbuvir x 12 weeks  
Viekira Pak + RBV x 12 weeks  
Sofosbuvir + simeprevir x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks  
Daclatasvir + sofosbuvir x 12 weeks | Elbasvir-grazoprevir + RBV x 16 weeks (if baseline NS5A RAVs are present) |
| Compensated Cirrhosis | Elbasvir-grazoprevir x 12 weeks (if no baseline NS5A RAVs)  
Ledipasvir-sofosbuvir x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks | Viekira Pak + RBV x 24 weeks  
Simeprevir + sofosbuvir ± RBV x 24 weeks (if no Q80K polymorphism)  
Daclatasvir + sofosbuvir ± RBV x 24 weeks  
Elbasvir-grazoprevir + RBV x 16 weeks (if baseline NS5A RAVs are present) |
| 1b Without Cirrhosis | Elbasvir-grazoprevir x 12 weeks  
Ledipasvir-sofosbuvir x 12 weeks  
Viekira Pak x 12 weeks  
Sofosbuvir + simeprevir x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks  
Daclatasvir + sofosbuvir x 12 weeks | None listed |
| Compensated Cirrhosis | Elbasvir-grazoprevir x 12 weeks  
Ledipasvir-sofosbuvir x 12 weeks  
Viekira Pak x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks | Daclatasvir + sofosbuvir ± RBV x 24 weeks  
Sofosbuvir + simeprevir ± RBV x 24 weeks |
| 2 Without Cirrhosis | Sofosbuvir-velpatasvir x 12 weeks | Daclatasvir + sofosbuvir x 12 weeks |
| Compensated Cirrhosis | Sofosbuvir-velpatasvir x 12 weeks | Daclatasvir + sofosbuvir x 16 to 24 weeks |
| 3 Without Cirrhosis | Daclatasvir + sofosbuvir x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks | None listed |
| Compensated Cirrhosis | Sofosbuvir-velpatasvir x 12 weeks  
Daclatasvir + sofosbuvir ± RBV x 24 weeks | None listed |
| 4 Without Cirrhosis | Technivie + RBV x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks  
Elbasvir-grazoprevir x 12 weeks  
Ledipasvir-sofosbuvir x 12 weeks | None listed |
| Compensated Cirrhosis | Technivie + RBV x 12 weeks  
Sofosbuvir-velpatasvir x 12 weeks  
Elbasvir-grazoprevir x 12 weeks  
Ledipasvir-sofosbuvir x 12 weeks | None listed |
| 5 or 6 With or without Cirrhosis | Sofosbuvir-velpatasvir x 12 weeks  
Ledipasvir-sofosbuvir x 12 weeks | None listed |

RBV = ribavirin; Technivie = ombitasvir, paritaprevir, and ritonavir; Viekira Pak = ombitasvir, paritaprevir, and ritonavir plus dasabuvir
- AASLD/IDSA guidelines state that patients with HCV/HIV coinfection should be treated similarly to non-coinfected patients; however, the potential for drug-drug interactions should be taken into consideration.

- Specific recommendations for treatment-experienced patients are based on HCV genotype, prior treatments received, and cirrhosis status.

- While guidelines recommend ledipasvir-sofosbuvir (Harvoni) for patients who have failed a sofosbuvir-based regimen, the recommendations are based on small pilot studies expert opinion only. There is currently no published, phase III data supporting the efficacy of ledipasvir-sofosbuvir (Harvoni) in patients who have failed prior therapy with a sofosbuvir-containing regimen. Additional studies are needed to identify the optimal regimen and duration.

**Safety** [5]

- The most common adverse events reported in clinical trials with ledipasvir-sofosbuvir (Harvoni) were headache and fatigue. Less than 1% of patients treated with ledipasvir-sofosbuvir (Harvoni) experienced anemia (an adverse event of interest in the treatment of HCV infection).

- Ledipasvir-sofosbuvir (Harvoni) is not associated with CYP 3A drug-drug interactions. It is a substrate of P-gp, so strong P-gp inducers (e.g. rifampin or St. John’s Wort) may decrease the plasma concentration of sofosbuvir.

- Post-marketing cases of symptomatic bradycardia have been reported when amiodarone is coadministered with a sofosbuvir-containing regimen in combination with an NS5A inhibitor, such as simeprevir. Co-administration of amiodarone with a sofosbuvir-containing regimen in combination with another direct-acting antiviral for HCV infection is not recommended.

**Dosing** [5]

- The recommended dosing for ledipasvir-sofosbuvir (Harvoni) is ledipasvir 90 mg-sofosbuvir 400 mg (one tablet) by mouth once daily with or without food.

- The duration of therapy with ledipasvir-sofosbuvir (Harvoni) is dependent on treatment experience and presence or absence of cirrhosis:
  * Treatment-naive patients with or without cirrhosis and treatment-experienced patients without cirrhosis: 12 weeks
  * Treatment-experienced patients with HCV genotype 1 and cirrhosis: 12 weeks in combination with ribavirin or 24 weeks.
Appendix 1: Direct-acting Antivirals for HCV

- boceprevir (Victrelis)
- daclatasvir (Daklinza)
- grazoprevir-elbasvir (Zepatier)
- ledipasvir-sofosbuvir (Harvoni)
- paritaprevir/ritonavir-ombitasvir (Technivie)
- paritaprevir/ritonavir-ombitasvir plus dasabuvir (Viekira Pak, Viekira XR)
- simeprevir (Olysio)
- sofosbuvir (Sovaldi)
- sofosbuvir-velpatasvir (Epclusa)
- telaprevir (Incivek)

Appendix 2: Definitions of Member Treatment History [7]

<table>
<thead>
<tr>
<th>Treatment-naive</th>
<th>Patients who have never received therapy for the treatment of hepatitis C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapser</td>
<td>Patients who had an undetectable HCV RNA level at the end of prior therapy with peginterferon and ribavirin, but had a subsequent detectable HCV RNA level during the follow-up period.</td>
</tr>
<tr>
<td>Partial responder</td>
<td>Patients who had a HCV RNA reduction of ≥ 2 log₁₀ after 12 weeks of prior therapy with peginterferon and ribavirin, but still had a detectable HCV RNA level during the treatment period.</td>
</tr>
<tr>
<td>Null responder</td>
<td>Patients who had a &lt; 2 log₁₀ reduction in HCV RNA after 12 weeks of prior therapy with peginterferon and ribavirin.</td>
</tr>
</tbody>
</table>

Cross References

- Daklinza™, daclatasvir, dru411
- Epclusa®, sofosbuvir-velpatasvir, dru457
- Olysio®, simeprevir, dru331
- Sovaldi®, sofosbuvir, dru332
- Technivie™, paritaprevir/ritonavir-ombitasvir, dru412
- Viekira Pak®, paritaprevir/ritonavir-ombitasvir plus dasabuvir, dru387
- Zepatier™, grazoprevir-elbasvir, dru435

Medical Policy Lab 47, Multianalyte Assays with Algorithmic Analysis for the Evaluation and Monitoring of Patients with Chronic Liver Disease
([http://blue.regence.com/trgmedpol/lab/lab47.pdf](http://blue.regence.com/trgmedpol/lab/lab47.pdf))
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References


Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
</tr>
</thead>
</table>
| 2/17/2017     | • Added additional investigational uses.  
• Clarified quantity limit for compensated cirrhosis. |
| 4/8/2016      | • Revised investigational uses.  
• Clarified coverage durations.  
• Added criteria for decompensated cirrhosis (Child-Pugh B and C)  
• Removed requirement for documentation that viral RNA is below the level of quantification after 8 weeks. |
| 2/12/2016     | • Removed requirement for advanced fibrosis, other end-organ disease manifestations, or other comorbid conditions.  
• Added requirement for documentation of pre-treatment viral RNA.  
• Reduced coverage duration for non-cirrhotic, treatment-naïve patients with pre-treatment viral RNA < 6 million to 8 weeks.  
• Added requirement for that Ledipasvir-sofosbuvir (Harvoni) will be used in combination with ribavirin for post-liver transplant patients and HCV Genotype 1 treatment-experienced cirrhotics.  
• Updated list of investigational uses. |
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|12/11/2015   | • Added coverage criteria for HCV genotypes 4, 5, and 6.  
• Added combination therapy with daclatasvir (Daklinza) as an investigational use.  
• Duration of coverage for treatment-experienced patients with HCV genotype 1 and cirrhosis is now limited to 12 weeks, unless there is documentation of HCV RNA below the lower limit of quantification after 8 or more weeks of treatment **and** documentation that ribavirin is contraindicated or not tolerated. |