Hepatitis C Direct Acting Antivirals
Prior Authorization with Quantity Limit Through Preferred Agent(s)

Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

This is a FlexRx standard and GenRx standard prior authorization program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

<table>
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<tr>
<th><strong>FDA APPROVED INDICATIONS AND DOSAGE</strong></th>
<th><strong>Agent</strong></th>
<th><strong>Indications</strong></th>
<th><strong>Dosage</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Daklinza™ (daclatasvir)</td>
<td>Oral tablet</td>
<td>● Treatment of chronic hepatitis C virus (HCV) genotype 1 or 3 infection in combination with sofosbuvir with or without ribavirin</td>
<td>60 mg tablet taken orally once daily with or without food in combination with sofosbuvir with or without ribavirin</td>
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<td></td>
<td></td>
<td>Limitations of Use: Sustained virologic response (SVR12) rates are reduced in genotype 3 patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks</td>
<td>Dose modification: Reduce dosage to 30 mg once daily with strong CYP3A inhibitors and increase dosage to 90 mg once daily with moderate CYP3A inducers</td>
</tr>
<tr>
<td>Epclusa® (sofosbuvir/velpatasvir)</td>
<td>Oral tablet</td>
<td>● Treatment of adult patients with chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection: - Without cirrhosis or with compensated cirrhosis - With decompensated cirrhosis in combination with ribavirin</td>
<td>1 tablet orally once daily containing 400 mg of sofosbuvir and 100 mg of velpatasvir for 12 weeks</td>
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<tr>
<td>Harvoni® (ledipasvir-sofosbuvir)</td>
<td>Oral tablet/Oral pellets</td>
<td>● Treatment of chronic hepatitis C in adults and pediatric patients 3 years of age and older: - For patients with genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis - For patients with genotype 1 infection</td>
<td>Adults: 1 tablet orally once daily containing 90 mg of ledipasvir and 400 mg of sofosbuvir. Length of therapy is dependent on genotype, patient treatment experience, and patient cirrhosis status. Pediatric 3 years of age and older:</td>
</tr>
</tbody>
</table>
| **Mavyret™**  
(glecaprevir/pibrentasvir) | ● Treatment of adult and pediatric patients 12 years and older or weighing at least 45 kg within chronic hepatitis C who have:  
- Genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child Pugh A)  
- Genotype 1 infection who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both  
Patients weighing less than 17 kg:  
One 33.75 mg/150 mg packet of pellets once daily  
Patients weighing 17 kg to less than 35 kg:  
One 45 mg/200 mg tablet once daily  
OR  
One 45 mg/200 mg packet of pellets once daily  
Patients weighing at least 35 kg:  
One 90 mg/400 mg tablet once daily  
OR  
Two 45 mg/200 mg tablets once daily  
OR  
Two 45 mg/200 mg packets of pellets once daily  
| **Olysio®**  
(simeprevir) | ● Treatment of adults with chronic HCV infection  
- In combination with sofosbuvir in patients with HCV genotype 1 without cirrhosis or with compensated cirrhosis  
- In combination with peg-interferon and ribavirin in patients with HCV genotype 1 or 4 without  
150 mg capsule taken orally once daily with food  

**Olysio®**  
(simeprevir)  
Oral capsule  

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| **Sovaldi® (sofosbuvir)**  
Oral tablet/Oral pellets | cirrhosis or with compensated cirrhosis (Child-Pugh A)  
Limitations of use:  
Efficacy of Olysio in combination with peg-interferon and ribavirin is substantially reduced in patients infected with HCV genotype 1a with an NS3 Q80K polymorphism  
Olysio is not recommended in patients who have previously failed therapy with a treatment regimen that included Olysio or other HCV protease inhibitors | **Adults:**  
1 tablet orally once daily containing 400 mg of sofosbuvir. Length of therapy is dependent on genotype, patient treatment experience, and patient cirrhosis status  
**Pediatric 3 years of age and older:**  
**Patients weighing less than 17 kg:**  
One 150 mg packet of pellets once daily  
**Patients weighing 17 kg to less than 35 kg:**  
One 200 mg tablet once daily  
OR  
One 200 mg packet of pellets once daily  
**Patients weighing at least 35 kg:**  
One 400 mg tablet once daily  
OR  
Two 200 mg tablets once daily  
OR  
Two 200 mg packets of pellets once daily |  
• Treatment of adult patients with chronic HCV genotype 1, 2, 3, or 4 infection without cirrhosis or with compensated cirrhosis as a component of a combination antiviral treatment regimen  
Treatment of pediatric patients 3 years of age and older with genotype 2 or 3 chronic HCV infection without cirrhosis or in combination with ribavirin for patients with compensated cirrhosis |
<table>
<thead>
<tr>
<th><strong>Technivie™</strong>&lt;br&gt;(ombitasvir/paritaprevir/ritonavir)</th>
<th><strong>Viekira Pak™</strong>&lt;br&gt;(ombitasvir/paritaprevir/ritonavir co-packaged with dasabuvir)</th>
<th><strong>Viekira XR™</strong>&lt;br&gt;(dasabuvir/ombitasvir/paritaprevir/ritonavir)</th>
<th><strong>Vosevi®</strong>&lt;br&gt;(sofosbuvir/velpatasvir/voxilaprevir)</th>
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<tr>
<td>Oral tablet</td>
<td>Treatment of adult patients with chronic hepatitis C virus who have:</td>
<td>Treatment of adult patients with chronic hepatitis C virus who have:</td>
<td>Treatment of adult patients with HCV infection without cirrhosis or compensated cirrhosis (Child-Pugh A) who have:</td>
</tr>
<tr>
<td>• Treatment of chronic hepatitis C genotype 4:</td>
<td>- Genotype 1b without cirrhosis or with compensated cirrhosis</td>
<td>- Genotype 1b without cirrhosis or with compensated cirrhosis</td>
<td>- Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor</td>
</tr>
<tr>
<td>- In combination with ribavirin for patients without cirrhosis or with compensated cirrhosis</td>
<td>- Genotype 1a without cirrhosis or with compensated cirrhosis used in combination with ribavirin</td>
<td>- Genotype 1a without cirrhosis or with compensated cirrhosis</td>
<td>- Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor</td>
</tr>
<tr>
<td>- Without ribavirin for treatment-naïve patients without cirrhosis who cannot take or tolerate ribavirin</td>
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</table>
Zepatier® (elbasvir/grazoprevir) | Treatment, with or without ribavirin, of chronic hepatitis C genotype 1 or 4 infection | 1 tablet (50 mg elbasvir and 100 mg grazoprevir) taken orally once daily for up to 16 weeks

Clinical Rationale

Hepatitis C is an infection of the liver caused by the Hepatitis C virus (HCV) and is one of the leading causes of chronic liver disease in the United States. According to the Centers for Disease Control and Prevention (CDC), there were an estimated 2.4 million people in the United States infected with hepatitis C as of 2016. Hepatitis C infection can either be acute or chronic. Acute HCV infection is defined as presenting within 6 months following exposure to the virus. The infection is defined as chronic if the virus is present beyond 6 months following exposure. 70% to 80% of those infected with HCV will go on to develop chronic HCV infection.13

Persons at high risk for contracting HCV infection include intravenous drug users, recipients of donated blood, blood products, and organs (now rare in the United States due to stringent blood screening), babies born to HCV infected mothers, and persons with HIV infection.13

Hepatitis C infection is asymptomatic in the early stages of the disease. However, with disease progression, patients may develop mild to severe chronic liver disease including cirrhosis and liver cancer. The goal of therapy is to eradicate the virus and prevent liver damage including cirrhosis. Direct acting antivirals (DAAs) are currently the mainstay of treatment for chronic HCV infection. Certain DAAs may be used as monotherapy while others require use in combination with other agents including peg-interferon, ribavirin and other DAAs.

The American Association of the Study of Liver Disease (AASLD) and the Infectious Disease Society of America (IDSA) have developed guidelines to aid in the management of hepatitis C. The guidelines address issues ranging from testing and linkage to care to the optimal treatment regimen based on patient situations.

AASLD/IDSA guidelines on when and in whom to treat12
The goal of therapy is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure. According to the AASLD/IDSA guidelines, treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Treatment should be initiated early because delaying therapy may decrease the benefits of eradicating the hepatitis C viral infection.

Although the prevalence of chronic HCV is lower in children than adults, an estimated 5 million children worldwide have active HCV infection. Data from the National Health and Nutrition Examination Survey (NHANES) collected between 2003 and 2010 indicates that 0.2% of 6 to 11 year olds (31,000 children) and 0.4% of 12 to 19 year olds (101,000 adolescents) in the US are chronically infected with HCV.

Birth to an HCV-infected mother is a known risk for infection and these children should be evaluated and tested for HCV. The rate of mother-to-child transmission (MTCT) of HCV infection is approximately 5%, although rates are higher among women with inadequately controlled HIV co-infection, and women with higher HCV-RNA levels, or viral loads (> 6 log IU/mL). Identifying, following, and treating exposed children is recommended. The basis for evaluation early in life is HCV-RNA testing, as maternal antibodies and consequently anti-HCV assay positivity may persist for 18 months. About 25% to 50% of infected infants spontaneously resolve HCV infection (loss of previously detectable HCV RNA) by 3 years of age. HCV RNA is more expensive than an antibody-based test; and there is no intervention or treatment that will occur prior to age 3—because of lack of approved drugs for this age group and to allow for possible spontaneous clearance.
New direct-acting antiviral agents (DAAs) capable of curing hepatitis C virus infection have been approved for use in the United States starting with the initial DAAs in 2011 and since that time many others have followed. DAAs offer the potential for highly effective, interferon-free (and in many cases, ribavirin-free) regimens for the majority of hepatitis C virus infected patients. Regimen selection varies by genotype and other patient factors, such as the presence of cirrhosis and treatment history. Patients who are co-infected with HCV and either hepatitis B or HIV should be treated as those mono-infected with HCV.

**Efficacy**

**Daklinza (daclatasvir)**

Daklinza is an HCV virus NS5A inhibitor indicated for use with sofosbuvir. The efficacy of Daklinza in combination with sofosbuvir with or without ribavirin for patients with HCV was evaluated in the ALLY-1, ALLY-2, and ALLY-3 trials.

ALLY-1, an open-label trial, included 113 patients with cirrhosis or recurrent infection after liver transplantation. Subjects with HCV genotype 1, 2, 3, 4, 5, or 6 were eligible to enroll although data on subjects with genotypes 2, 4, 5, or 6 was insufficient to provide recommendations. All subjects in the ALLY-1 trial received Daklinza in combination with sofosbuvir and ribavirin for 12 weeks. The primary outcome was sustained virologic response at 12 weeks following treatment (SVR12). SVR12 rates were comparable between genotype 1 and genotype 3. SVR12 ranged from 50% (for patients with Child-Pugh C) to 100% (for patients with genotype 1b).

ALLY-2 trial was an open-label trial evaluating the efficacy of Daklinza in combination with sofosbuvir in 153 HCV/HIV coinfected patients with chronic HCV genotype 1 to 6. Although this trial included patients with HCV genotype 1 to 6, this combination is FDA approved only for treatment of HCV genotype 1 and 3 therefore, clinical trial data for other genotypes will not be discussed here. Subjects with genotype 1 enrolled in the ALLY-2 trial received Daklinza plus sofosbuvir for 12 weeks. The primary outcome, overall SVR12, was 97% in genotype 1 patients. Patients with HCV genotype 1 and cirrhosis had a lower SVR12 (91%) as compared to those without cirrhosis (98%). SVR12 in genotype 3 patients was 100%.

The ALLY-3 trial was an open-label trial evaluating the efficacy of Daklinza in combination with sofosbuvir and ribavirin. The study enrolled 152 subjects with chronic hepatitis C genotype 3 infection and compensated liver disease. 101 subjects were treatment naïve, 7 subjects had been previously treated with a sofosbuvir regimen, and 2 subjects had previously received treatment with an investigational cyclophilin inhibitor. Subjects with previous exposure to an NS5A inhibitor (e.g. daclatasvir, ledipasvir, or ombitasvir) were excluded from the trial. The primary end-point, SVR 12, was 92% to 98% and 58% to 69% for patients without cirrhosis and for those with cirrhosis respectively. Relapse rates following completion of treatment were 9% to 14%.

**Epclusa**

Epclusa (sofosbuvir/velpatasvir) contains a hepatitis C nucleotide analog NS5B polymerase inhibitor (sofosbuvir) and a hepatitis C virus NS5A inhibitor (velpatasvir). Efficacy of this combination agent was evaluated in five phase 3 trials (ASTRAL-1, ASTRAL-2, ASTRAL-3, ASTRAL-4, and ASTRAL-5). All these trials included patients who were either treatment naïve or had previously been treated with an interferon based regimen (peginterferon plus ribavirin with or without a protease inhibitor). The primary endpoint for these trials was sustained virologic response at 12 weeks (SVR 12) following completion of therapy.

ASTRAL-1 was a placebo controlled trial that enrolled patients with HCV infection genotype 1, 2, 4, 5, or 6. Overall, the SVR 12 rate was 99% in patients who received Epclusa and 0% in those receiving placebo (95% confidence interval, p<0.001).

ASTRAL-2 and ASRTAL-3 were randomized, open label trials evaluating efficacy in patients with HCV genotype 2 or 3 respectively. Those with HCV genotype 2 received either Epclusa for 12 weeks or sofosbuvir plus ribavirin for 12 weeks. The SVR12 rates for the two treatment arms were 99% and 94% respectively. Subjects with HCV genotype 3 were randomized to receive either Epclusa for 12 weeks or sofosbuvir plus ribavirin for 24 weeks. The SVR 12 rates were 95% and 80% respectively.
ASTRAL-4 was an open label trial that evaluated efficacy of Epclusa in patients with decompensated cirrhosis. Patients were randomized to receive one of three treatment regimens: Epclusa for 12 weeks, Epclusa for 24 weeks, or Epclusa plus ribavirin for 12 weeks. SVR 12 rates were 83%, 86%, and 94% respectively.

ASTRAL-5 was an open-label trial that evaluated 12 weeks of Epclusa in patients with genotype 1, 2, 3, 4, 5, or 6 hepatitis C infection who were coinfected with HIV-1. The patients were all on antiretroviral therapy of various regimens. The primary endpoint was SVR12. The SVR12 ranged from 92-100% depending on genotype and in genotype 1 the subtype. No patient had HIV-1 rebound during treatment and CD4+ counts were stable during treatment.

**Harvoni**

Harvoni (ledipasvir/sofosbuvir) is a combination of an NS5A inhibitor (ledipasvir) and nucleotide analog NS5B polymerase inhibitor (sofosbuvir). Its efficacy was evaluated in several phase 2 and 3 clinical trials. These trials enrolled a broad range of patient populations including treatment naïve and treatment experienced patients, those without cirrhosis and with cirrhosis (compensated and decompensated), post-liver transplant patients, pediatric patients who were at least 3 years old or weighed more than 35 kg, as well as those with HIV/HCV co-infection. All the trials had a primary end point of sustained virologic response at 12 weeks (SVR12) following completion of treatment. Overall SVR12 was greater than 90% for the various patient populations. The treatment duration of this agent varies from 8 weeks to 24 weeks. Per the FDA labeling, treatment naïve patients with HCV genotype 1 with RNA of less than 6 million can be successfully treated with 8 weeks of Harvoni. This duration of treatment is not recommended in patients with cirrhosis, HIV, are post-liver transplantation, and/or black or African-American. Treatment experienced patients with cirrhosis may be treated with Harvoni alone for 24 weeks or in combination with ribavirin for 12 weeks. These two regimens are equally efficacious with SVR12 of 96% and 97% respectively.

**Mavyret**

Mavyret (glecaprevir/pibrentasvir) is a combination of an NS3/4A protease inhibitor (glecaprevir) and an NS5A inhibitor (pibrentasvir). Its safety and efficacy have been demonstrated in treatment naïve or patients previously treated with regimens containing peginterferon, ribavirin, and/or sofosbuvir (PRS) with HCV genotype 1, 2, 3, 4, 5 or 6 without cirrhosis or with compensated cirrhosis. Its safety and efficacy has also been demonstrated in patients who have previously been treated with a regimen containing an NS5A inhibitor or an NS3/4A protease inhibitor but not both. Patients with prior treatment with both an NS5A inhibitor and NS3/4A inhibitor were at an increased risk of virologic failure when retreated with Mavyret.

The efficacy of Mavyret in treatment naïve or PRS treatment experienced adults with HCV genotype 1, 2, 4, 5, or 6 infection without cirrhosis was evaluated in the ENDURANCE-1, ENDURANCE-4, SURVEYOR-1 (part 2), and SURVEYOR-2 (part 2 and part 4) trials. The SVR12 ranged from 93% to 100% depending on genotype. The EDNURANCE-1 trial demonstrated numerically similar efficacy in genotype 1 treatment naïve patients without cirrhosis treated for 8 weeks vs 12 weeks the SURVEYOR-2 trial also demonstrated very high SVR12 for genotypes 2, 4, 5, or 6 after 8 weeks of treatment. Therefore, the recommended length of therapy for treatment naïve patients without cirrhosis is 8 weeks.

The efficacy of Mavyret in treatment naïve or PRS treatment experienced adults with HCV genotypes 1, 2, 4, 5, or 6 infection with compensated cirrhosis was evaluated in the EXPEDITION-1 trial. Patients received Mavyret for 12 weeks. The SVR12 was 99-100% depending on genotype.

The efficacy of Mavyret in treatment naïve or PRS treatment experienced adults with HCV genotype 3 infection without cirrhosis or with compensated cirrhosis was evaluated in the ENDURANCE-3 and SURVEYOR-2 (part 3) trial. For patients without cirrhosis the SVR12 was numerically similar for patients without cirrhosis and the recommendation for these patients is to treat for 8 weeks. The overall SVR12 for all patients in these trials ranged from 94.9-98% depending on cirrhosis status and previous treatment.
The efficacy of Mavyret in treatment naïve and PRS treatment experienced adults with genotype 2, 4, 5, or 6 without cirrhosis was evaluated in the SURVEYOR-2 (part 2 and part 4), ENDURANCE-4, and SURVEYOR-1 (part 2) trials. SVR12 ranged from 93-100% depending on genotype.

The efficacy of Mavyret in treatment naïve or PRS treatment experienced adults with HCV genotype 1, 2, 4, 5, or 6 infection with compensated cirrhosis was evaluated in the EXPEDITION-1 trial. The SVR12 ranged from 99-100% depending on genotype.

The EXPEDITION-4 trial evaluated treatment naïve and PRS treatment experienced adults with chronic kidney disease stage 4 and 5 and chronic HCV infection without cirrhosis or with compensated cirrhosis. The overall SVR12 was 98%.

The MAGELLAN-1 trial evaluated adults who were NS5A inhibitor or NS3/4A protease inhibitor experienced patients without cirrhosis or with compensated cirrhosis. The SVR12 ranged from 92-94% depending on previous treatment.

The MAGELLAN-2 trial evaluated patients who were treatment-naïve or PRS treatment-experienced who have had a liver or kidney transplant. The overall SVR12 rate was 98%.

The efficacy of Mavyret was evaluated in an open-label study (DORA [Part 1]) that evaluated adolescent subjects 12 years to less than 18 years without cirrhosis who received Mavyret for 8 or 16 weeks. Treatment duration was chosen to match approved adult durations based on HCV genotype and prior treatment experience. The overall SVR12 rate was 100%.

**Olysio (simeprevir)**

Olysio is a HCV NS3/4A protease inhibitor. It is indicated for use in combination with sofosbuvir or in combination with ribavirin and peg-interferon (triple therapy). AASLD/IDSA no longer recommend use of simeprevir in combination with ribavirin and peg-interferon for genotype 1 patients due to low efficacy and high potential for side effects. The AASLD/IDSA guidelines do recommend Olysio as one of several potential regimens for patients with chronic kidney disease stage 1, 2, or 3.

**Sovaldi (sofosbuvir)**

Sovaldi is a nucleotide analog NS5B polymerase inhibitor. It is indicated for use in combination with other DAAs including daclatasvir and simeprevir. It may also be used in combination with peg-interferon and ribavirin. To date, sofosbuvir is the only oral DAA indicated for treatment of patients with hepatocellular carcinoma secondary to chronic HCV infection.

The safety and efficacy of Sovaldi was evaluated in five Phase 3 trials in a total of 1724 HCV mono-infected subjects with genotypes 1 to 6 chronic hepatitis C virus, one Phase 3 trial in 223 HSC/HIV-1 coinfected subjects with genotype 1, 2, or 3 HCV, and one trial in 106 pediatric subjects 3 years of age and older with genotype 2 or 3 HCV. The efficacy of Sovaldi (SVR12) is dependent on the combination regimen in which it is used, the patient’s genotype, and patient’s treatment history (range 82% - 100%).

The most common adverse events of sofosbuvir when used with ribavirin include fatigue headache and insomnia. Nausea, insomnia, and anemia were the most common adverse events when sofosbuvir was used in combination with ribavirin and peg-interferon.

**Technivie**

Technivie (ombitasvir/paritaprevir/ritonavir) is a combination therapy containing a hepatitis C virus NS5A inhibitor (ombitasvir), a hepatitis C virus NS3/4A protease inhibitor (paritaprevir), and a CYP3A inhibitor (ritonavir).

The efficacy of Technivie was evaluated in adults with chronic genotype 4 hepatitis C virus infection without cirrhosis in the PEARL-I trial. The patients were either treatment naïve or did not achieve a
virologic response with prior treatment with pegylated interferon/ribavirin. The primary outcome was SVR12. SVR 12 was 100% for treatment naïve and treatment experienced subjects whose regimen included ribavirin and 91% for treatment naïve patients whose regimen did not include ribavirin.

The efficacy of Technivie was evaluated in adults with chronic genotype 4 hepatitis C virus infection with compensated cirrhosis in the AGATE-I trial. The patients were either treatment naïve or were treatment experienced with peginterferon and ribavirin. Treatment Technivie and ribavirin for 16 weeks was not shown to increase SVR12 rates and therefore was not included in the results. The SVR12 was 97%.

Safety and efficacy of this combination regimen has not been studied in patients previously treated with a direct acting antiviral.

**Viekira Pak and Viekira XR**
Viekira Pak (ombitasvir/paritaprevir/ritonavir co-packaged with dasabuvir) and Viekira XR (dasabuvir/ombitasvir/paritaprevir/ritonavir) is a combination therapy containing a hepatitis C virus NS3/4A protease inhibitor (paritaprevir), a CYP3A inhibitor (ritonavir), a hepatitis C virus NS5A inhibitor (ombitasvir), and a hepatitis C NS5B palm polymerase inhibitor (dasabuvir). Safety and efficacy of this combination was evaluated in trials including treatment naïve, previous failures, cirrhotic and non-cirrhotic genotype 1 patients. The studies (SAPPHIRE-I, SAPPHIRE-II, PEARL-II, PEARL-III, PEARL-IV, TURQUOISE-II, AND TURQUOISE-III) all had a primary efficacy endpoint of SVR12.

Patients with genotype 1a infection without cirrhosis were evaluated in the SAPPHIRE-I, SAPPHIRE-II, and PEARL-IV trials. The SVR12 ranged from 95-97% depending on previous treatment.

Patients with genotype 1b infection without cirrhosis were evaluated in the PEARL-II and PEARL-III trials. SVR12 for both of these studies was 100%.

Patients with genotype 1a and genotype 1b infection with compensated cirrhosis were evaluated in the TURQUOISE-II and TURQUOISE-IV trials. The SVR12 ranged from 89-100% depending on genotype subtype and length of treatment.

Treatment guidelines recommend that patients that have failed a previous protease inhibitor containing regimen receive ledipasvir/sofosbuvir. Ombitasvir/paritaprevir/ritonavir + dasabuvir is not a recommended regimen in previous protease inhibitor failures due to risk of resistance.

**Vosevi**
Vosevi (sofosbuvir/velpatasvir/voxilaprevir) is a fixed-dose combination of a hepatitis C virus nucleotide analog NS5B polymerase inhibitor (sofosbuvir), an HCV NS5A inhibitor (velpatasvir), and an HCV NS3/4A protease inhibitor (voxilaprevir). Efficacy of this combination agent was evaluated in two phase 3 trials. The primary endpoint in both trials was SVR12.

The efficacy of Vosevi in patients with hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis who were treatment experienced with a NS5A inhibitor (POLARIS-1 trial). The SVR12 ranged from 91-100% depending on genotype.

The efficacy of Vosevi in patients with hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis who previously failed a hepatitis C direct acting antiviral (POLARIS-4 trial). The SVR12 ranged from 94-100% depending on genotype and in genotype 1, the subtype. Additional benefit of this combination agent over sofosbuvir/velpatasvir has not been shown in patients with genotype 1b, 2, 4, 5, or 6 infection who were previously treated with sofosbuvir without an NS5A inhibitor.

**Zepatier**
Zepatier (elbasvir/grazoprevir) is a combination regimen of an NS5A replication inhibitor (elbasvir) and an NS3/4A protease inhibitor (grazoprevir). Its efficacy was evaluated in several phase 2 and 3 clinical trials.
All the trials had a primary end point of sustained virologic response at 12 weeks (SVR12) following completion of treatment.

Efficacy of Zepatier in treatment naïve patients with HCV genotype 1 with or without cirrhosis was evaluated in the C-EDGE TN and C-EDGE COINFECTION trials. Subjects in both trials received Zepatier for 12 weeks. SVR12 was 95% in both trials. There were no significant differences in SVR12 between cirrhotic and non-cirrhotic patients. The C-EDGE TE trial evaluated efficacy of this combination in treatment experienced HCV genotype 1 patients with or without cirrhosis who had previously failed peginterferon plus ribavirin. Subjects received Zepatier monotherapy for 12 weeks or Zepatier with ribavirin for 16 weeks. SVR12 rates in the two treatment groups were 94% and 97% respectively.

Efficacy in HCV genotype 1 patients with or without cirrhosis who had previously failed peginterferon, ribavirin, plus a protease inhibitor was evaluated in the C-SALVAGE trial. This was an open label, single arm trial. All subjects received Zepatier plus ribavirin for 12 weeks. Overall SVR12 was 96%.

Efficacy of Zepatier in patients with HCV genotype 1 with or without cirrhosis and who had Chronic Kidney Disease (CKD) stage 4 (eGFR 15-29 mL/min/1.73 m²) or CKD Stage 5 (eGFR <15 mL/min/1.73 m²), including patients on hemodialysis was evaluated in the C-SURFER trial. Patients were randomized to receive either Zepatier for 12 weeks or placebo for 12 weeks followed by 12 weeks of Zepatier (deferred treatment group). Overall SVR12 was 99%. There were no significant differences with regard to safety in the Zepatier group versus placebo group.

These trials found that presence of NS5A amino acid polymorphisms in patients with HCV genotype 1a was associated with reduced efficacy of Zepatier regardless of treatment history or cirrhosis status. It is recommended to test for NS5A polymorphisms in HCV genotype 1a patients prior to starting treatment with this combination. If the polymorphism is present, addition of ribavirin to the treatment regimen and extension of the duration of treatment to 16 weeks is recommended.

Efficacy of Zepatier in HCV genotype 4 patients was evaluated in the C-SCAPE, C-EDGE TE, C-EDGE TN, and C-EDGE COINFECTION trials. Treatment naïve patients in these trials received Zepatier for 12 weeks while those who were treatment experienced received Zepatier plus ribavirin for 12 to 16 weeks. SVR12 in the treatment naïve and treatment experienced patients was 97% and 100% respectively.

Safety

Risk of Hepatitis B infection reactivation with HCV Direct Acting Antivirals

In October of 2016, the FDA issued a safety alert concerning risk of reactivation of hepatitis B viral (HBV) infection in patients treated with HCV direct acting antivirals (DAA). At the time of the alert, the FDA had identified 24 cases of HBV infection reactivation in patients who had been treated with a HCV DAA. In a few of these cases, the HBV reactivation resulted in serious liver problems or death. As a result, the FDA has required labeling for all HCV DAAs to include a boxed warning for HBV infection reactivation. In addition, the FDA has recommended that all patients be screened for evidence of current or prior HBV infection before starting treatment with HCV DAAs and be monitored for HBV reactivation during and after treatment with a HCV DAA.

References

# Hepatitis C Direct Acting Antivirals Prior Authorization with Quantity Limit – Through Preferred Agent(s)

## TARGET AGENTS

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<tr>
<th>Genotype</th>
<th>Preferred Agent(s)</th>
<th>Non-Preferred Agent(s)</th>
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<tbody>
<tr>
<td>1</td>
<td>Epclusa (sofosbuvir/velpatasvir) &lt;br&gt; Harvoni (ledipasvir/sofosbuvir)&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Ledipasvir/Sofosbuvir&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Sofosbuvir/Velpatasvir &lt;br&gt; Mavyret (glecaprevir/pibrentasvir) &lt;br&gt; Vosevi (sofosbuvir/velpatasvir)</td>
<td>Daklinza (daclatasvir) &lt;br&gt; Olysio (simeprevir) &lt;br&gt; Sovaldi (sofosbuvir)&lt;sup&gt;c&lt;/sup&gt; &lt;br&gt; Viekira PAK (ombitasvir/paritaprevir/ritonavir + dasabuvir) &lt;br&gt; Viekira XR (dasabuvir/ombitasvir/paritaprevir/ritonavir) &lt;br&gt; Zepatier (elbasvir/grazoprevir)&lt;sup&gt;d&lt;/sup&gt;</td>
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<tr>
<td>2</td>
<td>Epclusa (sofosbuvir/velpatasvir) &lt;br&gt; Sofosbuvir/Velpatasvir &lt;br&gt; Mavyret (glecaprevir/pibrentasvir) &lt;br&gt; Vosevi (sofosbuvir/velpatasvir)</td>
<td>Sovaldi (sofosbuvir)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Epclusa (sofosbuvir/velpatasvir) &lt;br&gt; Sofosbuvir/Velpatasvir &lt;br&gt; Mavyret (glecaprevir/pibrentasvir) &lt;br&gt; Vosevi (sofosbuvir/velpatasvir)</td>
<td>Daklinza (daclatasvir) &lt;br&gt; Sovaldi (sofosbuvir)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Epclusa (sofosbuvir/velpatasvir) &lt;br&gt; Harvoni (ledipasvir/sofosbuvir)&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Ledipasvir/Sofosbuvir&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Sofosbuvir/Velpatasvir &lt;br&gt; Mavyret (glecaprevir/pibrentasvir) &lt;br&gt; Vosevi (sofosbuvir/velpatasvir)</td>
<td>Olysio (simeprevir) &lt;br&gt; Sovaldi (sofosbuvir)&lt;sup&gt;c&lt;/sup&gt; &lt;br&gt; Technivie (ombitasvir/paritaprevir/ritonavir) &lt;br&gt; Zepatier (elbasvir/grazoprevir)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Epclusa (sofosbuvir/velpatasvir) &lt;br&gt; Harvoni (ledipasvir/sofosbuvir)&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Ledipasvir/Sofosbuvir&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Sofosbuvir/Velpatasvir &lt;br&gt; Mavyret (glecaprevir/pibrentasvir) &lt;br&gt; Vosevi (sofosbuvir/velpatasvir)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Epclusa (sofosbuvir/velpatasvir) &lt;br&gt; Harvoni (ledipasvir/sofosbuvir)&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Ledipasvir/Sofosbuvir&lt;sup&gt;b&lt;/sup&gt; &lt;br&gt; Sofosbuvir/Velpatasvir &lt;br&gt; Mavyret (glecaprevir/pibrentasvir) &lt;br&gt; Vosevi (sofosbuvir/velpatasvir)</td>
<td></td>
</tr>
</tbody>
</table>

---

a-Preferred agents will require prior authorization. The prior authorization for a specific agent will be based on the Food and Drug Administration (FDA) approved product labeling for the patient’s specific factors (e.g. genotype, cirrhosis status, treatment naïve vs. experienced, previous treatment)

b-Harvoni 8 week treatment is the preferred Harvoni regimen. For longer treatment durations (any genotype) Epclusa or Mavyret are preferred [depending on the Food and Drug Administration (FDA) approved product labeling for the patient’s specific factors (e.g. genotype, cirrhosis status, treatment naïve vs. experienced, previous treatment]

c-Sovaldi is non-preferred for patients without hepatocellular carcinoma. Exception made for patients with genotypes 2 or 3 who are at least 3 years of age to under 12 years of age or for patients < 45 kg.

## Brand (generic) | GPI | Multisource Code | Quantity Limit
---|---|---|---
Daklinza™ (daclatasvir) | 12353025100320 | M, N, O, or Y | 1 tablet/day
30 mg tablets | 12353025100330 | M, N, O, or Y | 1 tablet/day
60 mg tablets | 12353025100340 | M, N, O, or Y | 1 tablet/day
90 mg tablets |
<table>
<thead>
<tr>
<th>Product Name</th>
<th>Dosage Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epclusa® (sofosbuvir/velpatasvir)</td>
<td>400 mg sofosbuvir/100 mg velpatasvir tablets 12359902650330 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td>Harvoni® (ledipasvir/sofosbuvir)</td>
<td>33.75 mg/150 mg packet with oral pellets TBD M, N, O, or Y 1 packet/day</td>
</tr>
<tr>
<td></td>
<td>45 mg/200 mg tablets 12359902400310 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td></td>
<td>45 mg/200 mg packet with oral pellets TBD M, N, O, or Y 1 packet/day</td>
</tr>
<tr>
<td></td>
<td>90 mg ledipasvir/ 400 mg sofosbuvir tablets 12359902400320 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir</td>
<td>90 mg ledipasvir/ 400 mg sofosbuvir tablets 12359902400320 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td>Mavyret™ (glecaprevir/pibrentasvir)</td>
<td>100 mg glecaprevir/40 mg pibrentasvir tablets 12359902350320 M, N, O, or Y 3 tablets/day</td>
</tr>
<tr>
<td>Olysio® (simeprevir)</td>
<td>150 mg capsule 12353077100120 M, N, O, or Y 1 capsule/day</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td>400 mg sofosbuvir/ 100 mg velpatasvir tablets 12359902650330 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td>Sovaldi® (sofosbuvir)</td>
<td>150 mg packet with oral pellets TBD M, N, O, or Y 1 packet/day</td>
</tr>
<tr>
<td></td>
<td>200 mg tablets 12353080000310 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td></td>
<td>200 mg packet with oral pellets TBD M, N, O, or Y 1 packet/day</td>
</tr>
<tr>
<td></td>
<td>400 mg tablets 12353080000320 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td>Technivie™ (ombitasvir/paritaprevir/ritonavir)</td>
<td>12.5/75/50 mg ombitasvir/paritaprevir/ritonavir tablets 12359903600320 M, N, O, or Y 2 tablets/day</td>
</tr>
<tr>
<td>Viekira PAK™ (ombitasvir/paritaprevir/ritonavir + dasabuvir)</td>
<td>12.5/75/50 mg ombitasvir/paritaprevir/ritonavir + 250 mg dasabuvir tablets 1235990460B720 M, N, O, or Y 1 pack (112 tablets)/28 days</td>
</tr>
<tr>
<td>Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir)</td>
<td>200 mg/8.33 mg/50 mg/33.33 mg dasabuvir/ombitasvir/paritaprevir/ritonavir tablets 12359904607530 M, N, O, or Y 3 tablets/day</td>
</tr>
<tr>
<td>Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)</td>
<td>400 mg sofosbuvir/100 mg velpatasvir/100 mg voxilaprevir tablets 12359903800330 M, N, O, or Y 1 tablet/day</td>
</tr>
<tr>
<td>Zepatier® (elbasvir/grazoprevir)</td>
<td>50 mg elbasvir/100 mg grazoprevir tablets 12359902300320 M, N, O, or Y 1 tablet/day</td>
</tr>
</tbody>
</table>

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**

Daklinza™ (daclatasvir) Evaluation

Daklinza™ (daclatasvir) will be approved when ALL of the following are met:

1. **ONE** of the following:
   - There is documentation that the patient is currently using the requested agent
   **OR**
   - The patient is new to therapy and **ALL** of the below:
     i. The patient has a diagnosis of chronic hepatitis C genotype 1 or 3  **AND**
     ii. **ONE** of the following:
        1. The patient is treatment naïve  **OR**
        2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin
iii. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection

iv. If the HBV screening was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent

v. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis

2. ONE of the following:
   A. The patient is currently being treated with the non-preferred agent
   OR
   B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, treatment naive vs treatment experienced, previous treatment)
   OR
   C. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s)

3. The patient does not have any FDA labeled contraindications to the requested agent

4. ONE of the following:
   A. If the patient is also receiving a strong CYP3A inhibitor, the requested dose is Daklinza 30mg daily
   OR
   B. If the patient is also receiving a moderate CYP3A inducer, the requested dose is Daklinza 90 mg daily
   OR
   C. Daklinza 60 mg daily

5. The requested agent will be used in a treatment regimen as noted in Table 1 (FDA labeling)

6. The length of therapy requested is recommended for the patient’s genotype as noted in Table 1 (FDA labeling)

7. The requested quantity (dose) does NOT exceed the program quantity limit

Length of Approval: Up to the duration of treatment determined in Table 1

Table 1: Sovaldi and Daklinza Combination Treatment Recommendations Based on FDA Labeling

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient population</th>
<th>Treatment</th>
<th>Duration of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Without cirrhosis</td>
<td>Daklinza + Sovaldi</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Compensated (Child-Pugh A) cirrhosis</td>
<td>Daklinza + Sovaldi</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Decompensated (Child-Pugh B or C) cirrhosis</td>
<td>Daklinza + Sovaldi + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Post-transplant</td>
<td>Daklinza + Sovaldi + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Without cirrhosis</td>
<td>Daklinza + Sovaldi</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Compensated (Child-Pugh A) cirrhosis</td>
<td>Daklinza + Sovaldi + ribavirin</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>Decompensated (Child-Pugh B or C) cirrhosis</td>
<td>Daklinza + Sovaldi + ribavirin</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>Post-transplant</td>
<td>Daklinza + Sovaldi + ribavirin</td>
<td>12 weeks</td>
<td></td>
</tr>
</tbody>
</table>

*HCV/HIV co-infection, follow recommendations in table above

**Epclusa and Sofosbuvir/Velpatasvir Evaluation**

*Epclusa or Sofosbuvir/Velpatasvir* will be approved when ALL of the following are met:

1. ONE of the following is met:
   A. There is documentation that the patient is currently using the requested agent  **OR**
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6  **AND**
      ii. ONE of the following:
         1. The patient is treatment naïve  **OR**
         2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin with or without an HCV protease inhibitor  **AND**
      iii. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection  **AND**
      iv. If the screening for HBV was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent  **AND**
      v. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis  **AND**

2. The patient does not have any FDA labeled contraindications to the requested agent  **AND**

3. The dose is within the FDA labeled dose  **AND**

4. The requested agent will be used in a treatment regimen noted in Table 2 (FDA labeling)  **AND**

5. The length of therapy requested is recommended for the patient’s genotype as noted in Table 2 (FDA labeling)  **AND**

6. The requested quantity (dose) does NOT exceed the program quantity limit

**Length of Approval:** Up to the duration of treatment as determined in Table 2

**Table 2: Epclusa or Sofosbuvir/Velpatasvir Treatment Recommendations based on FDA labeling**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient population*</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 2, 3, 4, 5, or 6</td>
<td>Patients without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Epclusa</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Patients with decompensated cirrhosis (Child-Pugh B and C)</td>
<td>Epclusa + ribavirin</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

---

*HCV/HIV co-infection, follow recommendations in table above
* HCV/HIV-1 co-infection, follow recommendations in table above

**Harvoni and Ledipasvir/Sofosbuvir Evaluation**

**Harvoni or Ledipasvir/Sofosbuvir** will be approved when ALL of the following are met:

1. ONE of the following is met:
   A. There is documentation that the patient is currently using the requested agent
   OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1, 4, 5, or 6
      AND
      ii. The prescriber has provided the patient’s baseline HCV RNA level if the patient has genotype 1
      AND
      iii. ONE of the following:
           1. The patient is treatment naïve
           OR
           2. The patient was previously treated (i.e. treatment experienced) with peg-interferon and ribavirin with or without an HCV protease inhibitor
      AND
      iv. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection
      AND
      v. If the screening for HBV was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
      AND
      iv. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis
      AND
      v. ONE of the following:
         1. The requested length of therapy is 8 weeks
         OR
         2. The patient is a pediatric patient AND ONE of the following:
            a. The patient is ≥ 3 years of age and < 12 years of age AND weighs < 45 kg
            OR
            b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Mavyret
            OR
            c. The prescriber has submitted information supporting the use of the requested agent over Mavyret (e.g., the patient is currently taking the requested agent)
         OR
         3. The patient is an adult AND ONE of the following:
            a. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to BOTH Epclusa and Mavyret
            OR
            b. The prescriber has submitted information supporting the use of the requested agent over BOTH Epclusa and Mavyert (e.g., the patient is currently taking the requested agent)

   AND
   2. The patient does not have any FDA labeled contraindications to the requested agent
   AND
   AND
   3. The dose is within the FDA labeled dose
4. The requested agent will be used in a treatment regimen as noted in Table 3 (FDA labeling)

5. The length of therapy requested is recommended for the patient’s genotype as noted in Table 3 (FDA labeling)

6. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
   OR
   B. The requested agent is Harvoni 45 mg/200 mg oral pellets AND BOTH of the following:
      i. The requested quantity (dose) does NOT exceed 2 packets daily
      AND
      ii. The prescriber has submitted information stating why the patient cannot take 1 tablet of Harvoni 90 mg/400 mg strength
   OR
   C. The requested agent is Harvoni 45 mg/200 mg tablet AND BOTH of the following:
      i. The requested quantity (dose) does NOT exceed 2 tablets daily
      AND
      ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: Up to the duration of treatment as determined in Tables 3

Table 3: Harvoni or Ledipavir/Sofosbuvir Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients 3 years of age and older*</th>
<th>Treatment</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Treatment-naïve with initial viral load of &lt; 6 M IU/mL and without cirrhosis, HIV infection, history of liver transplantation and/or are not black or African-American</td>
<td>Harvoni</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1</td>
<td>Treatment-experienced (^9) without cirrhosis</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced (^9) with compensated cirrhosis (Child-Pugh A) and eligible for ribavirin</td>
<td>Harvoni + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced (^9) with compensated cirrhosis (Child-Pugh A) and ineligible for ribavirin (^h)</td>
<td>Harvoni</td>
<td>24 weeks</td>
</tr>
<tr>
<td></td>
<td>Treatment-naïve and treatment-experienced (^9) with decompensated cirrhosis (Child-Pugh B or C)</td>
<td>Harvoni + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1 or 4</td>
<td>Treatment-naïve and treatment-experienced (^9) liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>4, 5, or 6</td>
<td>Treatment-naïve and treatment-experienced (^9) without cirrhosis or</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
e - HCV/HIV-1 co-infection, follow recommendation in table above

f - Treatment-experienced - patients who have failed therapy with either peg-interferon + ribavirin or a HCV protease inhibitor + peginterferon + ribavirin.

h - Ribavirin ineligible - patients with history of intolerance, contraindication, or hypersensitivity to ribavirin

**Mavyret Evaluation**

**Mavyret** will be approved when ALL of the following are met:

1. ONE of the following is met:
   A. There is documentation that the patient is currently using the requested agent
   OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6
      AND
      ii. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection
      AND
      iii. If the screening for HBV was positive for current or prior HBV infection, the
          prescriber will monitor the patient for HBV flare-up or reactivation during and after
          treatment with the requested agent
      AND
      iv. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a
          specialist in the area of the patient’s diagnosis
      AND
      v. The patient has not been previously treated with the requested agent

2. The patient does not have any FDA labeled contraindications to the requested agent

3. The dose is within the FDA labeled dose

4. The requested agent will be used in a treatment regimen noted in Table 4 (FDA labeling)

5. The length of therapy requested is recommended for the patient’s genotype as noted in Table 4 (FDA labeling)

6. The requested quantity (dose) does NOT exceed the program quantity limit

**Length of Approval**: Up to the duration of treatment as determined in Table 4

**Table 4: Mavyret Treatment Recommendations based on FDA labeling**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population - adults and pediatric patients 12 years of age or older or weighing at least 45 kg (^{e,i})</th>
<th>Treatment</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver or kidney transplant recipients</td>
<td>Mavyret</td>
<td>No Cirrhosis</td>
</tr>
<tr>
<td>1, 2, 3, 4, 5, or 6</td>
<td></td>
<td></td>
<td>12 weeks</td>
</tr>
<tr>
<td>1</td>
<td>Liver or kidney transplant recipients who are treatment experienced with an NS5A inhibitor but without prior</td>
<td>Mavyret</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>
treatment with an NS3/4A protease inhibitor (PI) |  |  
--- | --- | ---
3 | Liver or kidney transplant recipients who are treatment experienced with PRS | Mavyret | 16 weeks | 16 weeks
1, 2, 3, 4, 5, or 6 | Treatment naïve | Mavyret | 8 weeks | 8 weeks
1 | Treatment experienced with an NS5A inhibitor but without prior treatment with an NS3/4A protease inhibitor (PI) | Mavyret | 16 weeks | 16 weeks
1 | Treatment experienced with an NS3/4A protease inhibitor but without prior treatment with an NS5A inhibitor | Mavyret | 12 weeks | 12 weeks
1, 2, 4, 5, or 6 | Treatment experienced with PRS | Mavyret | 8 weeks | 12 weeks
3 | Treatment experienced with PRS | Mavyret | 16 weeks | 16 weeks

e - HCV/HIV-1 co-infection, follow recommendations in table above
i - Patients with any degree of kidney impairment (including those on hemodialysis), follow recommendations in table above
j - Examples of HCV NS5A inhibitors include daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir
k - Examples of NS3/4A protease inhibitors include simeprevir, boceprevir, telaprevir
I - PRS=Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor

**Olysio (simeprevir) Evaluation**

Olysio® (simeprevir) will be approved when ALL of the following are met:

1. ONE of the following:
   A. There is documentation that the patient is currently using the requested agent
   OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1 or 4
      AND
      ii. If requesting Olysio to be used with peg-interferon and ribavirin for genotype 1a, the patient does not have NS3 Q80K polymorphism
      AND
      iii. ONE of the following:
         1. The patient is treatment naïve
         OR
         2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin
         AND
      iv. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection
      AND
      v. If the HBV screening was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
      AND
      vi. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis
      AND

2. ONE of the following:
   A. The patient is currently being treated with the non-preferred agent
   OR
B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL of the preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, treatment naive vs treatment experienced, previous treatment)  
OR  
C. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s)  

AND  
3. The patient does not have any FDA labeled contraindications to the requested agent  
AND  
4. The dose is within the FDA labeled dose  
AND  
5. The requested agent will be used in a treatment regimen noted in Table 5 or 6 (FDA labeling)  
AND  
6. The length of therapy requested is recommended for the patient’s genotype as noted in Table 6 or 7 (FDA labeling)  
AND  
7. The requested quantity (dose) does NOT exceed the program quantity limit

**Length of Approval:** Up to the duration of treatment as determined in Table 5 or 6

### Table 5: Olysio and Sovaldi Combination Therapy Treatment Recommendations Based on FDA Labeling

<table>
<thead>
<tr>
<th>Genotype and Patient Population</th>
<th>Treatment regimen and duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 treatment naive and treatment-experienced&lt;sup&gt;m,n,o,p,q,r&lt;/sup&gt; patients without Cirrhosis</td>
<td>12 weeks of Olysio + Sovaldi</td>
</tr>
<tr>
<td>Genotype 1 treatment naive and treatment-experienced&lt;sup&gt;m,n,o,p,q,r&lt;/sup&gt; patients with compensated Cirrhosis (Child-Pugh A)</td>
<td>24 weeks of Olysio + Sovaldi</td>
</tr>
</tbody>
</table>

- Treatment-experienced patients include prior relapers, partial responders and prior null responders who failed peg-interferon plus ribavirin and peg-interferon intolerant patients  
- Prior relapse: HCV RNA not detected at the end of prior IFN based therapy and HCV RNA detected during follow up  
- Partial responder: Prior on-treatment ≥ 2 log₁₀ IU/mL reduction in HCV RNA from baseline at week 12 and HCV RNA detected at the end of prior IFN based therapy  
- Null responder: Prior on treatment < 2 log₁₀ reduction in HCV RNA from baseline at week 12 during prior IFN based therapy  
- Interferon ineligible is defined as one or more of the following:
  - Intolerance to interferon  
  - Autoimmune hepatitis and other autoimmune disorders  
  - Hypersensitivity to PEG interferon or any of its components  
  - Decompensated hepatic disease  
  - Major uncontrolled depressive illness  
  - A baseline neutrophil count below 1500/µL  
  - A baseline platelet count below 90,000/µL  
  - A baseline hemoglobin below 10 g/dL  
  - A history of preexisting cardiac disease  

- Intolerance is defined by Prime as intolerance to the drug and/or excipients, not the route of administration including patients who have previously discontinued therapy with IFN due to adverse events (e.g. hypersensitivity, anaphylaxis, severe rash, severe anemia)

### Table 6: Olysio, Peg-interferon (PEG-IFN), and Ribavirin Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient population</th>
<th>Treatment regimen</th>
<th>Duration of therapy</th>
</tr>
</thead>
</table>
| 1 or 4   | Treatment naive and prior relapsers<sup>n</sup> HCV monoinfected patients without cirrhosis or with compensated cirrhosis (Child-Pugh A) | Olysio + PEG-IFN + RBV | Olysio: 12 weeks  
PEG-IFN: 24 weeks |
Treatment naïve and prior relapers\(^n\) with HCV/HIV co-infected patients without cirrhosis

<table>
<thead>
<tr>
<th></th>
<th>Olysio + PEG-INF + RBV</th>
<th>Olysio: 12 weeks PEG-INF: 24 weeks</th>
</tr>
</thead>
</table>

Treatment naïve and prior relapers\(^n\) with HCV/HIV co-infection with compensated cirrhosis (Child-Pugh A)

<table>
<thead>
<tr>
<th></th>
<th>Olysio + PEG-INF + RBV</th>
<th>Olysio: 12 weeks PEG-INF: 48 weeks</th>
</tr>
</thead>
</table>

Prior non-responders (including partial\(^o\) and null responders\(^p\)) without cirrhosis or with compensated cirrhosis (Child-Pugh A) and with or without HIV co-infection

<table>
<thead>
<tr>
<th></th>
<th>Olysio + PEG-INF + RBV</th>
<th>Olysio: 12 weeks PEG-INF: 48 weeks</th>
</tr>
</thead>
</table>

\(n\) - Prior relapse: HCV RNA not detected at the end of prior IFN based therapy and HCV RNA detected during follow up.

\(o\) - Partial responder: Prior on-treatment ≥ 2 log10 IU/mL reduction in HCV RNA from baseline at week 12 and HCV RNA detected at the end of prior IFN based therapy.

\(p\) - Null responder: Prior on treatment < 2 log 10 reduction in HCV RNA from baseline at week 12 during prior IFN based therapy.

Sovaldi (sofosbuvir) Evaluation

Sovaldi\(^\circledR\) (sofosbuvir) will be approved when ALL of the following are met:

1. ONE of the following:
   A. There is documentation that the patient is currently using the requested agent
      OR
   B. The patient is new to therapy and ALL of the below:
      i. ONE of the following:
         1. The patient is a pediatric patient with chronic hepatitis C genotype 2 or 3 AND ONE of the following:
            a. The patient has a diagnosis or hepatocellular carcinoma secondary to chronic hepatitis C genotype 2 or 3
               OR
            b. The patient is ≥ 3 years of age and < 12 years of age AND weighs < 45 kg
               OR
            c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Mavyret
               OR
            d. The prescriber has submitted information supporting the use of the requested agent over Mavyret (e.g., the patient is currently taking the requested agent)
   OR

2. The patient is an adult and has a diagnosis of hepatocellular carcinoma secondary to chronic hepatitis C genotype 1, 2, 3, or 4
   OR

3. The patient is an adult and has a diagnosis of chronic hepatitis C genotype 1, 2, 3, or 4 without hepatocellular carcinoma AND ONE of the following:
   a. The patient is currently being treated with the non-preferred agent
   OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
   OR
c. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s)

AND

ii. ONE of the following:
   1. The patient is treatment naïve
      OR
   2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin

AND

iii. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection

AND

iv. If the HBV screening was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent

AND

v. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis

AND

2. The patient does not have any FDA labeled contraindications to the requested agent

AND

3. The dose is within the FDA labeled dose

AND

4. The requested agent will be used in a treatment regimen noted in Table 7 or 8 (FDA labeling)

AND

5. The length of therapy requested is recommended for the patient’s genotype as noted in Table 7 or 8 (FDA labeling)

AND

6. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
   B. The requested agent is Sovaldi 200 mg oral pellets AND BOTH of the following:
      i. The requested quantity (dose) does NOT exceed 2 packets daily
      AND
      ii. The prescriber has submitted information stating why the patient cannot take 1 tablet of Sovaldi 400 mg strength
      OR
   C. The requested agent is Sovaldi 200 mg tablets AND BOTH of the following:
      i. The requested quantity (dose) does NOT exceed 2 tablets daily
      AND
      ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of approval: Up to the duration of treatment as determined in Table 7 or 8

Table 7: Sovaldi Treatment Recommendations in Adult Patients with Genotype 1, 2, 3, or 4 Based on FDA Labeling

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Treatment</th>
<th>Duration of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 or 4 treatment naïve without cirrhosis or with</td>
<td>Sovaldi + Peg-interferon alfa + ribavirin</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
compensated cirrhosis (Child-Pugh A)

<table>
<thead>
<tr>
<th>Genotype 1 treatment naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A) (interferon ineligible\textsuperscript{q,r})</th>
<th>Sovaldi + ribavirin</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 2 treatment naïve or treatment experienced\textsuperscript{s} without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Sovaldi + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 3 treatment naïve or treatment experienced\textsuperscript{s} without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Sovaldi + ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>1-4 with hepatocellular carcinoma awaiting liver transplantation</td>
<td>Sovaldi + ribavirin</td>
<td>Up to 48 weeks</td>
</tr>
</tbody>
</table>

\textsuperscript{e} – HCV/HIV-1 co-infection, follow recommendations in table above

\textsuperscript{q} - Interferon ineligible is defined as one or more of the following:

- Intolerance to interferon
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to PEG interferon or any of its components
- Decompensated hepatic disease
- Major uncontrolled depressive illness
- A baseline neutrophil count below 1500/µL
- A baseline platelet count below 90,000/µL
- A baseline hemoglobin below 10 g/dL
- A history of preexisting cardiac disease

\textsuperscript{r} - Intolerance is defined by Prime as intolerance to the drug and/or excipients, not the route of administration including patients who have previously discontinued therapy with IFN due to adverse events (e.g. hypersensitivity, anaphylaxis, severe rash, severe anemia)

\textsuperscript{s} – Treatment experienced patients who have failed an interferon based regimen with or without ribavirin

**Table 8: Sovaldi and Ribavirin with or without Peg-interferon Treatment Recommendations for Pediatric Patients 3 Years of Age and Older Based on FDA Labeling**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient population\textsuperscript{*}</th>
<th>Treatment</th>
<th>Duration of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Treatment-naïve and treatment experienced\textsuperscript{s} without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Sovaldi + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Treatment-naïve and treatment experienced\textsuperscript{s} without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Sovaldi + ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>2 or 3</td>
<td>Pediatric patients with hepatocellular carcinoma awaiting liver transplantation</td>
<td>Sovaldi + ribavirin</td>
<td>48 weeks</td>
</tr>
</tbody>
</table>

\textsuperscript{e} – HCV/HIV-1 co-infection, follow recommendations in table above

\textsuperscript{s} – Treatment experienced patients who have failed an interferon based regimen with or without ribavirin

**Technivie Evaluation**

Technivie (ombitasvir/paritaprevir/ritonavir) will be approved when ALL the following are met:

1. ONE of the following:
   A. There is documentation that the patient is currently using the requested agent
OR

B. The patient is new to therapy and ALL of the below:
   i. The patient has a diagnosis of chronic hepatitis C, genotype 4
      AND
      i. ONE of the following:
         1. The patient is treatment naive
         OR
         2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin
      AND
      ii. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection
      AND
      iii. If the HBV screening was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
      AND
      iv. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis

2. ONE of the following:
   A. The patient is currently being treated with the non-preferred agent
   OR
   B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
   OR
   C. The prescriber has provided information in support of the use of the non-preferred agent over the preferred agent(s)

AND

3. The patient does not have any FDA labeled contraindications to the requested agent

AND

4. The dose is within the FDA labeled dose

AND

5. The requested agent will be used in a treatment regimen noted in Table 9 (FDA labeling)

AND

6. The length of therapy requested is recommended for the patient’s genotype as noted in Table 9 (FDA labeling)

AND

7. The requested quantity (dose) does NOT exceed the program quantity limit

Length of Approval:  Up to the duration of treatment as determined by Table 9

Table 9: Technivie Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Treatment</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 4 without cirrhosis and the patient ribavirin eligible</td>
<td>Technivie + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 4, treatment naïve, without cirrhosis and the patient ribavirin ineligible\</td>
<td>Technivie</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
Genotype 4 with compensated cirrhosis

Technivie + ribavirin

12 weeks

e - HCV/HIV-1 co-infection, follow recommendations in table above
h - Ribavirin ineligible - patients with history of intolerance, contraindication, or hypersensitivity to ribavirin

**Viekira Pak and Viekira XR Evaluation**

**Viekira PAK or Viekira XR** will be approved when ALL of the following are met:

1. ONE of the following is met:
   
   A. There is documentation that the patient is currently using the requested agent **OR**
   
   B. The patient is new to therapy and ALL of the below:
      
      i. The patient has a diagnosis of chronic hepatitis C genotype 1 **AND**
      
      ii. The prescriber has provided the patient’s subtype **AND**
      
      iii. ONE of the following:
         
         1. The patient is treatment naïve **OR**
         
         2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin **AND**
         
      iv. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection **AND**
         
      v. If the HBV screening was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent **AND**
         
      vi. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis **AND**

2. ONE of the following:
   
   A. The patient is currently being treated with the non-preferred agent **OR**
   
   B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, renal function, treatment naïve vs treatment experienced, previous treatment) **OR**
   
   C. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s) **AND**

3. The patient does not have any FDA contraindications to the requested agent **AND**

4. The dose is within the FDA labeled dose **AND**

5. The requested agent will be used in a treatment regimen noted in Table 10 (FDA labeling) **AND**

6. The length of therapy requested is recommended for the patient’s genotype as noted in Table 10 (FDA labeling) **AND**

7. The requested quantity (dose) does NOT exceed the program quantity limit

**Length of Approval:** Up to the duration as determined in Table 10
Table 10: Viekira PAK and Viekira XR Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a, without cirrhosis</td>
<td>Viekira PAK + ribavirin OR Viekira XR + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a, with compensated cirrhosis</td>
<td>Viekira PAK + ribavirin OR Viekira XR + ribavirin</td>
<td>24 weeks t</td>
</tr>
<tr>
<td>Genotype 1b, with or without compensated cirrhosis</td>
<td>Viekira PAK OR Viekira XR</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a or 1b post liver transplant with normal hepatic function (i.e. Metavir ≤2)</td>
<td>Viekira PAK + ribavirin OR Viekira XR + ribavirin</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

e - HCV/HIV-1 co-infection, follow recommendations in table above  
t - Viekira PAK or Viekira XR with RBV for 12 weeks may be considered for some patients based on prior treatment history. The SVR12 rate difference between 24 and 12 weeks of treatment was +6% with differences varying by pretreatment history.

Vosevi Evaluation

Vosevi will be approved when ALL of the following are met:

1. ONE of the following is met:
   A. There is documentation that the patient is currently using the requested agent
   OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6  
      AND
      ii. If genotype 1, the prescriber has provided the patient’s subtype  
      AND
      iii. The patient is NOT treatment naïve  
      AND
      iv. The patient has NOT been previously treated with the requested agent  
      AND
      v. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection  
      AND
      vi. If the screening for HBV was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent  
      AND
      vii. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis

2. The patient does not have any FDA labeled contraindications to the requested agent

3. The dose is within the FDA labeled dose

4. The requested agent will be used in a treatment regimen noted in Table 11

5. The length of therapy requested is recommended for the patient’s genotype as noted in Table 11(FDA labeling)

6. The requested quantity (dose) does NOT exceed the program quantity limit

Length of Approval: Up to the duration of treatment as determined in Table 11
Table 11: Vosevi Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Patients Previously Treated with an HCV Regimen Containing:</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1,2,3,4,5, or 6 without cirrhosis or with compensated cirrhosis (Child Pugh A)</td>
<td>An NS5A inhibitor$^j$</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a or 3 without cirrhosis or with compensated cirrhosis (Child Pugh A)</td>
<td>Sofosbuvir without an NS5A inhibitor$^u$</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

$^e$ - HCV/HIV-1 co-infection, follow recommendations in table above
$^j$ - Examples of HCV NS5A inhibitors include daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir
$^u$ - Sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (simeprevir)

**Zepatier Evaluation**

**Zepatier** will be approved when ALL of the following are met:

1. ONE of the following is met:
   A. There is documentation that the patient is currently using the requested agent  
      **OR**
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1 or 4  
      **AND**
      ii. BOTH of the following:
          1. If genotype 1, the prescriber has provided the patient’s subtype  
             **AND**
          2. If the subtype 1a, the prescriber has tested the patient for NS5A polymorphisms  
      **AND**
      iii. ONE of the following:
           1. The patient is treatment naïve  
              **OR**
           2. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin with or without an HCV protease inhibitor  
      **AND**
      iv. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection  
      **AND**
      v. If the screening for HBV was positive for current or prior HBV infection, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent  
      **AND**
      vi. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis  
      **AND**

2. ONE of the following:
   A. The patient is currently being treated with the non-preferred agent  
      **OR**
   B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)  
      **OR**
   C. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s)  
      **AND**
3. The patient does not have any FDA labeled contraindications to the requested agent
   AND
4. The dose is within the FDA labeled dose
   AND
5. The requested agent will be used in a treatment regimen noted in Table 12 (FDA labeling)
   AND
6. The length of therapy requested is recommended for the patient’s genotype as noted in Table 12
   (FDA labeling)
   AND
7. The requested quantity (dose) does NOT exceed the program quantity limit

**Length of Approval:** Up to the duration of treatment as determined in Table 12

**Table 12: Zepatier Treatment Recommendations based on FDA labeling**

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a*:</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>(Treatment-naive or PegIFN/RBV-experienced <strong>without</strong> baseline NSSA polymorphisms)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 1a*:</td>
<td>Zepatier + ribavirin</td>
<td>16 weeks</td>
</tr>
<tr>
<td>(Treatment-naive or PegIFN/RBV-experienced <strong>with</strong> baseline NSSA polymorphisms)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 1b:</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>(Treatment-naive or PegIFN/RBV-experienced)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 1a or 1b:</td>
<td>Zepatier + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>(PegIFN/RBV/protease inhibitor-experienced)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 4:</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>(Treatment-naive)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype 4:</td>
<td>Zepatier + ribavirin</td>
<td>16 weeks</td>
</tr>
<tr>
<td>(PegIFN/RBV-experienced)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* - HCV/HIV-1 co-infection, follow dosage recommendations in the table above

v - Genotype 1a: Testing for the presence of virus with NSSA resistance-associated polymorphisms is recommended

w - Polymorphisms at amino acid positions 28, 30, 31, or 93

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**

**New to market chronic Hepatitis C agents** will be approved when ALL of the following are met:

1. ONE of the following is met:
   A. There is documentation that the patient is currently using the requested agent
   OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has an FDA approved diagnosis for the requested agent
         AND
      ii. The requested agent is FDA approved for treatment of the patient’s genotype
         AND
      iii. If FDA labeling for the requested agent requires patients are tested for hepatitis B viral (HBV) infection prior to starting treatment with the requested agent BOTH of the following:
          1. The prescriber has screened the patient for current or prior HBV
             AND
          2. If the HBV screening was positive for current or prior HBV, the prescriber will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
             AND
          iv. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. gastroenterologist, hepatologist, or infectious disease) or has consulted with a specialist in the area of the patient’s diagnosis
             AND
      2. The patient does not have any FDA labeled contraindications to the requested agent
         AND
3. ONE of the following:
   A. The requested agent is a preferred agent
   OR
   B. The patient is currently being treated with the non-preferred agent
   OR
   C. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL preferred agent(s) for the patient’s specific factors (e.g., genotype, cirrhosis status, renal function, treatment naïve vs treatment experienced, previous treatment)
   OR
   D. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s)

4. The dose is within the FDA labeled dose

5. The requested agent will be used in a treatment regimen noted in Table 13 (FDA labeling)

6. The length of therapy requested is recommended for the patient’s diagnosis, and genotype as noted in Table 13 (FDA labeling)

7. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
   OR
   B. BOTH of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: Up to the duration of treatment as determined in Table 13

Table 13: Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>FDA approved indication(s)</th>
<th>Genotype</th>
<th>Treatment Regimen</th>
<th>FDA labeled dose</th>
<th>Treatment Duration</th>
</tr>
</thead>
</table>
Step Therapy Supplement
Program Summary

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   OR

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

   OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria