# Hepatitis C Second Generation Antivirals Prior Authorization Through Preferred Agent(s) Program Summary

## FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indications</th>
<th>Dose and Interval</th>
</tr>
</thead>
</table>
| **Epclusa** (sofosbuvir/velpatasvir) | Treatment of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection:  
- without cirrhosis or with compensated cirrhosis  
- with decompensated cirrhosis (use in combination with ribavirin) | 1 tablet orally once daily containing 400 mg of sofosbuvir and 100 mg of velpatasvir for 12 weeks |
| **Harvoni** (ledipasvir-sofosbuvir) | Treatment, with or without ribavirin, of adults with chronic hepatitis C, genotype 1, 4, 5, or 6 infection  
Treatment of pediatric patients 12 years of age or older or weighing at least 35 kg with chronic hepatitis C, genotype 1, 4, 5, or 6 without or with compensated cirrhosis | 1 tablet orally once daily containing 90 mg of ledipasvir and 400 mg of sofosbuvir for up to 24 weeks |
| **Technivie** (ombitasvir/paritaprevir/ritonavir) | Treatment, in combination with ribavirin, of chronic hepatitis C genotype 4 without cirrhosis or with compensated cirrhosis | Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) for 12 weeks |
| **Viekira Pak** (paritaprevir/ritonavir/ombitasvir and dasabuvir) | Treatment of adult patients with chronic hepatitis C virus:  
- genotype 1b with or without compensated cirrhosis  
- genotype 1a with or without compensated cirrhosis. Use in combination with ribavirin for genotype 1a | Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) and one dasabuvir 250 mg tablet twice daily (morning and evening) for up to 24 weeks |
| **Viekira XR** (dasabuvir/ombitasvir/paritaprevir/ritonavir) | Treatment of adult patients with chronic hepatitis C virus:  
- genotype 1b with or without compensated cirrhosis  
- genotype 1a with or without compensated cirrhosis. Use in combination with ribavirin for genotype 1a | 3 tablets taken once daily for up to 24 weeks |
| **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) once daily for up to 16 weeks |
Disease Background\textsuperscript{5,6}

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 3.5 million people infected with hepatitis C as of 2015. 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. 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. 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 treat\textsuperscript{5}

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.

Treatment recommendations for patients who have failed therapy with the newer DAAs is limited. AASLD/IDSA recommend ledipasvir/sofosbuvir plus ribavirin for 24 weeks for those who have cirrhosis and have failed sofosbuvir plus ribavirin with or without peg-interferon. Deferral of treatment is recommended, pending availability of data, for patients who have failed other DAAs (not including protease inhibitors). If the decision is made to treat urgently, resistance testing should guide selections of the appropriate therapy for treatment.

AASLD recommends awaiting availability of pangenotypic agents for the management of patients with mixed genotypes. Patients who are co-infected with HCV and either hepatitis B or HIV should be treated as those mono-infected with HCV.

Elbasvir/grazoprevir\textsuperscript{4}

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 this combination 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 elbasvir/grazoprevir 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 elbasvir/grazoprevir monotherapy for 12
weeks or elbasvir/grazoprevir 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 elbasvir/grazoprevir plus ribavirin for 12 weeks. Overall SVR12 was 96%.

Efficacy of this combination 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 elbasvir/grazoprevir for 12 weeks or placebo for 12 weeks followed by 12 weeks of elbasvir/grazoprevir (deferred treatment group). Overall SVR12 was 99%. There were no significant differences with regard to safety in the elbasvir/grazoprevir 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 elbasvir/grazoprevir 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 this combination 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 elbasvir/grazoprevir for 12 weeks while those who were treatment experienced received elbasvir/grazoprevir plus ribavirin for 12 to 16 weeks. SVR12 in the treatment naïve and treatment experienced patients was 97% and 100% respectively.

The most common adverse events observed with elbasvir/grazoprevir were fatigue, headache, and nausea. This combination is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C). Use in combination with strong CPY3A inducers, efavirenz, or organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors is contraindicated.

Ledipasvir/sofosbuvir

Ledipasvir/sofosbuvir is a combination of an NS5A inhibitor and nucleotide analog NS5B polymerase inhibitor. 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, 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 ledipasvir/sofosbuvir. This duration of treatment is not recommended in patients with cirrhosis, HIV, and/or are post-liver transplantation. Treatment experienced patients with cirrhosis may be treated with ledipasvir/sofosbuvir 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.¹

The most common side effects associated with ledipasvir/sofosbuvir are fatigue, headache, and asthenia.

Ombitasvir/paritaprevir/ritonavir and dasabuvir³,8

Safety and efficacy of this combination was evaluated in 4 pivotal trials including treatment naïve, previous failures, cirrhotics and non-cirrhotic genotype 1 patients. The studies (Sapphire I, Turquoise II, Pearl III and Pearl IV) all had a primary efficacy endpoint of a sustained virologic response (SVR) at 12 weeks after the end of therapy. Sapphire I was conducted in treatment naïve patients without cirrhosis. Turquoise-2 was conducted in treatment naïve and previously treated patients and included cirrhotic patients. Pearl III evaluated treatment naïve genotype 1b patients and Pearl IV evaluated treatment naïve
genotype 1a patients. SVR rates in these trials ranged from 90% to 99%. 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.

**Ombitasvir/paritaprevir/ritonavir**

Efficacy and safety of this combination, when used with or without ribavirin, was evaluated in a single clinical trial (PEARL-I). The study enrolled 135 subjects with chronic hepatitis C (HCV) infection genotype 4 without cirrhosis. The subjects were either treatment naïve or had history of virologic failure following treatment with pegylated interferon and ribavirin. The primary end point of the study was sustained virologic response at 12 weeks (SVR 12) following completion of therapy. 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. Safety and efficacy of this combination regimen has not been studied in patients previously treated with a direct acting antiviral.

The most common adverse events reported in the trial were asthenia, fatigue, nausea, insomnia, pruritis, and skin reaction. These adverse events were graded as mild in severity.

**Sofosbuvir/velpatasvir**

Efficacy of this combination agent was evaluated in four phase 3 trials (ASTRAL-1, ASTRAL-2, ASTRAL-3, and ASTRAL-4). 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 sofosbuvir/velpatasvir 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 sofosbuvir/velpatasvir 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 sofosbuvir/velpatasvir 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 sofosbuvir/velpatasvir in patients with decompensated cirrhosis. Patients were randomized to receive one of three treatment regimens: sofosbuvir/velpatasvir for 12 weeks, sofosbuvir/velpatasvir for 24 weeks, or sofosbuvir/velpatasvir plus ribavirin for 12 weeks. SVR 12 rates were 83%, 86%, and 94% respectively.

The most common adverse events reported in patients who received sofosbuvir/velpatasvir were headache and fatigue. Those with decompensated cirrhosis who were treated with sofosbuvir/velpatasvir and ribavirin reported fatigue, anemia, nausea, headache, insomnia, and diarrhea as the most common adverse events.

**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 Second Generation Antivirals Prior Authorization - Through Preferred Oral agent(s)

OBJECTIVE
The intent of the Hepatitis C second generation antiviral Prior Authorization (PA) program is to appropriately select patients for therapy according to the Food and Drug Administration (FDA) approved product labeling and/or clinical guidelines and/or clinical studies. If the client has preferred agent(s), a preferred agent may be approved for use once all criteria have been met; a non-preferred agent may be approved if the patient is currently treated with the non-preferred agent or the prescriber has provided documentation in support of use of the non-preferred agent over the preferred agent.

TARGET DRUGS
Preferred Agent(s) as determined by client
Epclusa® (sofosbuvir/velpatasvir) (preferred for genotype 2 and 3)
Harvoni® (ledipasvir/sofosbuvir) (preferred for genotype 1, 4, 5, and 6)

Non-preferred Agent(s) as determined by client
Technivie™ (ombitasvir/paritaprevir/ritonavir)
Viekira Pak™ (ombitasvir/paritaprevir/ritonavir + dasabuvir)
Viekira XR™ (dasabuvir/ombitasvir/paritaprevir/ritonavir)
Zepatier™ (elbasvir/grazoprevir)

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epclusa®(sofosbuvir/velpatasvir)</td>
<td>12359902650330</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Harvoni® (ledipasvir/sofosbuvir)</td>
<td>12359902400320</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Technivie™ (ombitasvir/paritaprevir/ritonavir)</td>
<td>12359903600320</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Viekira PAK™ (ombitasvir/paritaprevir/ritonavir + dasabuvir)</td>
<td>1235990460B720</td>
<td>M, N, O or Y</td>
</tr>
<tr>
<td>Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir)</td>
<td>12359904607530</td>
<td>M, N, O or Y</td>
</tr>
<tr>
<td>Zepatier™ (elbasvir/grazoprevir)</td>
<td>12359902300320</td>
<td>M, N, O, or Y</td>
</tr>
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</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Epclusa will be approved when ALL of the following criteria are met:
1. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 AND
2. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent AND
3. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND
4. The patient does not have any FDA labeled contraindications to the requested agent AND
5. ONE of the following:
   a. The patient is treatment naïve OR
   b. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin with or without an HCV protease inhibitor AND
6. The dose is within the FDA labeled dose AND
7. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient’s genotype as noted in Table 1 (FDA labeling)

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

Table 1: Epclusa 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>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Harvoni will be approved when ALL of the following criteria are met:
1. The patient has a diagnosis of chronic hepatitis C genotype 1, 4, 5, or 6 AND
2. The prescriber has provided the patient’s baseline HCV RNA level if the patient has genotype 1 AND
3. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent AND
4. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND
5. The patient does not have any FDA labeled contraindications to the requested agent AND
6. ONE of the following:
   a. The patient is treatment naïve OR
   b. The patient was previously treated (i.e. treatment experienced) with ONLY ONE of the following regimens:
      i. The previous treatment is peg-interferon and ribavirin with or without an HCV protease inhibitor OR
      ii. The previous treatment is Sovaldi and ribavirin with or without peg-interferon and the patient has BOTH of the following:
         1. Genotype 1 AND
         2. Cirrhosis AND
7. The dose is within the FDA labeled dose AND
8. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient’s genotype as noted in Table 2 and 3 (FDA labeling) and Table 4 (AASLD/IDSA guidelines)

Length of approval: Up to the duration of treatment as determined in Tables 2, 3, and 4.
### Table 2: Harvoni Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Adult Patient Population^</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 any of the following: cirrhosis, HIV infection, or history of liver transplantation</td>
<td>Harvoni</td>
<td>8 weeks*</td>
</tr>
<tr>
<td>1</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** without cirrhosis</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1</td>
<td>Treatment-experienced** with compensated cirrhosis (Child-Pugh A) and eligible for ribavirin</td>
<td>Harvoni + ribavirin</td>
<td>12 weeks†</td>
</tr>
<tr>
<td>1</td>
<td>Treatment-experienced** with compensated cirrhosis (Child-Pugh A) and ineligible for ribavirin£</td>
<td>Harvoni</td>
<td>24 weeks</td>
</tr>
<tr>
<td>1</td>
<td>Treatment-naïve and treatment-experienced** 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** 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** without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

### Table 3: Harvoni Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Pediatric Patients ≥ 12 years of Age or Weighing at Least 35 Kg^</th>
<th>Treatment</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</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¥ without cirrhosis</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1</td>
<td>Treatment-experienced¥ with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>24 weeks</td>
</tr>
<tr>
<td>4, 5, or 6</td>
<td>Treatment-naïve and treatment experienced¥, without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>Harvoni</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
Table 4: Harvoni Treatment Recommendations based on AASLD/IDSA Guidelines

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patient Population^</th>
<th>Treatment</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cirrhosis and history of treatment failure with Sovaldi plus ribavirin with or without peg-interferon</td>
<td>Harvoni + ribavirin</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

^HCV/HIV co-infected patients: Follow the dosage recommendation in the table above unless otherwise noted.
*8 weeks may be considered in treatment naive patients without cirrhosis, without HIV infection, or without history of liver transplantation who have pre-treatment HCV RNA < 6 million IU/mL. For this patient population Prime is requiring 8 weeks of therapy.
**Treatment-experienced - patients who have failed therapy with either peg-interferon + ribavirin or a HCV protease inhibitor + peginterferon + ribavirin.
† Harvoni + ribavirin for 12 weeks can be considered in treatment-experienced HCV genotype 1 patients with cirrhosis who are eligible for ribavirin. For this patient population Prime will require treatment with Harvoni in combination with ribavirin for 12 weeks unless the patient is ineligible to receive ribavirin.
£ Ribavirin ineligible - patients with history of intolerance, contraindication, or hypersensitivity to ribavirin
¥ Treatment-experienced patients who have failed an interferon based regimen with or without ribavirin

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Technivie (ombitasvir/paritaprevir/ritonavir) will be approved when ALL of the following criteria are met:
1. The patient has a diagnosis of compensated chronic hepatitis C, genotype 4
   AND
2. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
   AND
3. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist
   AND
4. The patient does not have any FDA labeled contraindications to the requested agent
   AND
5. ONE of the following:
   a. The patient is treatment naïve OR
   b. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin
   AND
6. The dose is within the FDA labeled dose
   AND
7. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient’s genotype as noted in Table 5 (FDA labeling)

Length of approval: Up to the duration of treatment as determined by Table 5

Table 5: 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>
<tr>
<td>Genotype 4 with compensated cirrhosis</td>
<td>Technivie + ribavirin</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
*Ribavirin ineligible - patients with history of intolerance, contraindication, or hypersensitivity to ribavirin

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Viekira PAK and Viekira XR will be approved when ALL of the following criteria are met:

1. The patient has a diagnosis of compensated chronic hepatitis C genotype 1 AND
2. The prescriber has provided the patient’s subtype AND
3. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent AND
4. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND
5. The patient does not have any FDA contraindications to the requested agent AND
6. ONE of the following:
   a. The patient is treatment naïve OR
   b. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin
7. The dose is within the FDA labeled dose
8. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient’s genotype as noted in Table 6 (FDA labeling)

Length of approval: Up to the duration as determined in Table 6

Table 6: 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</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Viekira XR + ribavirin</td>
<td></td>
</tr>
<tr>
<td>Genotype 1a, with compensated cirrhosis</td>
<td>Viekira PAK + ribavirin OR</td>
<td>24 weeks**</td>
</tr>
<tr>
<td></td>
<td>Viekira XR + ribavirin</td>
<td></td>
</tr>
<tr>
<td>Genotype 1b, with or without compensated cirrhosis</td>
<td>Viekira PAK OR</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>Viekira XR</td>
<td></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</td>
<td>24 weeks</td>
</tr>
<tr>
<td></td>
<td>Viekira XR + ribavirin</td>
<td></td>
</tr>
</tbody>
</table>

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

**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.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

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

1. The patient has a diagnosis of compensated chronic hepatitis C genotype 1 or 4 AND
2. BOTH of the following:
   a. If genotype 1, the prescriber has provided the patient’s subtype AND
   b. If the subtype 1a, the prescriber has tested the patient for NS5A polymorphisms AND
3. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent AND
4. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND
5. The patient does not have any FDA labeled contraindications to the requested agent AND
6. ONE of the following:
   a. The patient is treatment naïve OR
   b. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin with or without an HCV protease inhibitor AND
7. The dose is within the FDA labeled dose AND
8. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient’s genotype as noted in Table 7 (FDA labeling)

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

### Table 7: 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: Treatment-naive or PegIFN/RBV-experienced without baseline NS5A polymorphisms(^\dagger)</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a: Treatment-naive or PegIFN/RBV-experienced with baseline NS5A polymorphisms(^\dagger)</td>
<td>Zepatier + ribavirin</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Genotype 1b: Treatment-naive or PegIFN/RBV-experienced</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a or 1b: PegIFN/RBV/protease inhibitor-experienced</td>
<td>Zepatier + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 4: Treatment-naive</td>
<td>Zepatier</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 4: PegIFN/RBV-experienced</td>
<td>Zepatier + ribavirin</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>

\(^\dagger\) Polymorphisms at amino acid positions 28, 30, 31, or 93
\(^\#\) Genotype 1a: Testing for the presence of virus with NS5A resistance-associated polymorphisms is recommended.
\(^\$\) HCV/HIV co-infection and/or cirrhosis: follow dosage recommendations in the table above

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**

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

1. The patient has an FDA approved diagnosis for the requested agent AND
2. BOTH of the following:
   a. FDA labeling for the requested agent requires patients are tested for hepatitis B viral (HBV) infection prior to starting treatment with the requested agent AND
   b. The prescriber has screened the patient for current or prior HBV and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent AND
3. The requested agent is FDA approved for treatment of the patient’s genotype AND
4. The patient does not have any FDA labeled contraindications to the requested agent AND
5. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND
6. The dose is within the FDA labeled dose AND
7. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient’s diagnosis, and genotype as noted in Table 8 (FDA labeling)

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

### Table 8: Treatment Recommendations based on FDA labeling

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>FDA approved</th>
<th>Genotype</th>
<th>Treatment</th>
<th>FDA labeled</th>
<th>Treatment</th>
</tr>
</thead>
</table>

Choice_PS_HepC_SecGen_PA_ProgSum_AR0716_r0517
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PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Non-Preferred Agent(s) will be approved when the drug specific criteria above and ONE of the following additional criteria are met:

1. The patient is currently being treated with the non-preferred agent OR
2. The patient has an FDA labeled contraindication or hypersensitivity to the preferred agent(s) OR
3. If requesting Zepatier, the patient has severe renal impairment (i.e. stage 4 or 5 Chronic Kidney disease as indicated by eGFR of <30 mL/min/1.73 m²) or end stage renal disease requiring hemodialysis OR
4. The prescriber has submitted documentation in support of the use of the non-preferred agent, over the preferred agent(s)

Contraindications:

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>Contraindication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epclusa® (sofosbuvir/velpatasvir)</td>
<td>Epclusa and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated</td>
</tr>
<tr>
<td>Harvoni® (ledipasvir/sofosbuvir)</td>
<td>If used in combination with ribavirin, all contraindications to ribavirin also apply to Harvoni combination therapy.</td>
</tr>
<tr>
<td>Technivie™ (paritaprevir/ritonavir/ombitasvir)</td>
<td>Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)]. Co-administration with drugs that are: highly dependent on CYP3A for clearance; moderate and strong inducers of CYP3A. Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Steven-Johnson syndrome). The contraindications to ribavirin also apply to this combination regimen (Technivie + ribavirin).</td>
</tr>
<tr>
<td>Viekira PAK™ (paritaprevir/ritonavir/ombitasvir + dasabuvir) and Viekira XR™ (dasabuvir/ombitasvir/paritaprevir/ritonavir)</td>
<td>Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)]. Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Steven-Johnson syndrome). Co-administration with drugs that are: highly dependent on CYP3A for clearance; moderate or strong inducers of CYP3A and strong inducers of CYP2C8; and strong inhibitors of CYP2C8. If Viekira or Viekira XR is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen.</td>
</tr>
<tr>
<td>Zepatier™ (elbasvir/grazoprevir)</td>
<td>Patients with moderate or severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)]. Organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors, strong CYP3A inducers, and efavirenz. If Zepatier is administered with ribavirin, the contraindications to ribavirin also apply.</td>
</tr>
</tbody>
</table>