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

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

FDA APPROVED INDICATIONS [1-7]

Agent(s)	Indication(s)
Epclusa® (sofosbuvir/velpatasvir) Oral tablet	Treatment of adult and pediatric patients 3 years of age and older 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
Harvoni® (ledipasvir-sofosbuvir) Oral tablet/Oral pellets	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 with decompensated cirrhosis in combination with ribavirin - For patients with genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis in combination with ribavirin
Mavyret® (glecaprevir/pibrentasvir) Oral tablet	Treatment of adult and pediatric patients 3 years and older with chronic hepatitis C who have: - Genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Turcotte-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
Sovaldi® (sofosbuvir) Oral tablet	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

Oral pellets	Treatment of pediatric patients 3 years of age and older with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin
Viekira Pak® (ombitasvir/paritaprevir/ritonavir co-packaged with dasabuvir) Oral tablets	Treatment of adult patients with chronic hepatitis C virus who have: - Genotype 1b without cirrhosis or with compensated cirrhosis - Genotype 1a without cirrhosis or with compensated cirrhosis used in combination with ribavirin
Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) Oral tablet	Treatment of adult patients with HCV infection without cirrhosis or compensated cirrhosis (Child-Turcotte-Pugh A) who have: - Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor - Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor
Zepatier® (elbasvir/grazoprevir) Oral tablet	Treatment of chronic hepatitis C genotype 1 or 4 infection in adult and pediatric patients 12 years of age and older or weighing at least 30 kg. Zepatier is indicated for use with ribavirin in certain patient populations

Clinical Rationale

Hepatitis C is an infection of the liver caused by the Hepatitis C virus (HCV), a blood-borne virus. Today, most people become infected with HCV by sharing needles or other equipment to inject drugs. Hepatitis C infection can either be acute or chronic. Acute HCV infection is defined as presenting within 6 months following exposure to the virus. In 2018, the reported acute hepatitis C case count in the United States corresponded to a rate of 1.2 cases per 100,000 population, an over 71% increase from the reported incidence rate in 2014. The infection is defined as chronic if the virus is present beyond 6 months following exposure. More than 50% of people who become infected with HCV develop chronic infection. Chronic hepatitis C is a serious disease that can result in cirrhosis, liver cancer, and death.[9]

The American Association for the Study of Liver Diseases (AASLD) along with the Infectious Diseases Society of America (IDSA) recommend the following:[8]

- One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years and older
- One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection
- Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy
- Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure
- Annual HCV testing is recommended for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP)

Risk activities:

- Injection drug use (current or ever, including those who injected only once)
- Intranasal illicit drug use
- Use of glass crack pipes
- Male engagement in sex with men
- Engagement in chem sex (defined as the intentional combining of sex with the use of particular nonprescription [illicit] drugs in order to facilitate or enhance the sexual encounter)

Risk exposures:
- Persons on long-term hemodialysis (ever)
- Persons with percutaneous/parenteral exposures in an unregulated setting
- Healthcare, emergency medical, and public safety workers after needlestick, sharps, or mucosal exposure to HCV-infected blood
- Children born to HCV-infected women
- Recipients of a prior transfusion or organ transplant, including persons who:
    - Were notified that they received blood from a donor who later tested positive for HCV
    - Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
    - Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated

Other conditions and circumstances:
- HIV infection or HBV infection
- Sexually active persons about to start pre-exposure prophylaxis (PrEP) for HIV
- Chronic liver disease and/or chronic hepatitis, including unexplained elevated alanine aminotransferase (ALT) levels
- Solid organ donors (living and deceased) and solid organ transplant recipients

AASLD/IDSA guidelines on when and in whom to initiate HCV therapy
The goal of treatment of HCV-infected persons 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 as evidenced by a sustained virologic response (SVR) (defined as the continued absence of detectable HCV RNA for at least 12 weeks after completion of therapy). According to the AASLD/IDSA guidelines, treatment is recommended for all patients with acute or 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 SVR and increase the rates of liver-related mortality.[8]

Although the prevalence of chronic HCV is lower in children than adults, an estimated 3.5-5 million children worldwide have chronic 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 HCV antibody positive.[11]

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 (greater than 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.[11]

Simplified Treatment[12]

Direct-acting antiviral agents (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.

The National Academies of Science, Engineering, and Medicine have proposed a strategy to reduce cases of chronic HCV infection by 90% by 2030. Data shows that HCV treatment can be effectively provided by a broad range of health care professionals with differing expertise – including specialists, primary care physicians, nurse practitioners, clinical pharmacy specialists, physician assistants, and registered nurses-without compromising treatment efficacy or safety. AASLD/IDSA has created simplified regimens to treat HCV in adults without cirrhosis or compensated cirrhosis who have not been previously treated for their infection to allow for the expansion of healthcare professionals who prescribe antiviral therapy and increase the number of persons treated. These simplified treatment algorithms are designed to be used by any health care provider knowledgeable about HCV disease and treatment, including those without extensive experience, who have timely access to a specialist. Any patients not included in the simplified treatment regimens should be seen by a specialist.

For patients without cirrhosis, the pretreatment evaluation should include:

- Calculate fibrosis-4 (FIB-4) score
- Cirrhosis assessment (liver biopsy is not required – a patient is presumed to have cirrhosis if they have a FIB-4 score greater than 3.25 or any of the following findings from a previously performed test
    - Transient elastography indicating cirrhosis (e.g., FibroScan stiffness greater than 12.5 kPa)
    - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (e.g., FibroSure, Enhanced Liver Fibrosis Test)
    - Clinical evidence of cirrhosis (e.g., liver nodularity and/or splenomegaly on imaging, platelet count less than 150,000/mm^3)
    - Prior liver biopsy showing cirrhosis
- Medication reconciliation
- Potential drug-drug interactions assessment
- Patient education about proper administration of medications, adherence, and prevention of reinfection

Patients without cirrhosis who have any of the following are NOT eligible for simplified treatment:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- Hepatitis B surface antigen (HBsAg) positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

The recommended treatment regimens are glecaprevir (300 mg)/pibrentasvir (120 mg) taken with food for 8 weeks or sofosbuvir (400 mg)/velpatasvir (100 mg) for a duration of 12 weeks.

For patients with compensated cirrhosis (Child-Turcotte-Pugh class A), the pretreatment evaluation should include:

- Calculate FIB-4 score (liver biopsy not required)
- Calculate Child-Turcotte-Pugh (CTP) score
- Ultra-sound imaging of the liver within the prior 6 months to evaluate for hepatocellular carcinoma (HCC) and sub clinical ascites
- Medication reconciliation
- Potential drug-drug interaction assessment
- Patient education about proper administration of medications, adherence, and prevention of reinfection

- Pretreatment laboratory testing:
    - Within 3 months of initiating treatment:
        - Complete blood count (CBC)
        - International normalized ratio (INR)
        - Hepatic function panel (i.e., albumin, total and direct bilirubin, ALT, AST)
        - Calculated glomerular filtration rate (eGFR)
    - Any time prior to starting antiviral therapy:
        - Quantitative HCV-RNA (HCV viral load)
        - HIV antigen/antibody test
        - Hepatitis B surface antigen
        - HCV genotype (if treating with sofosbuvir/velpatasvir)
    - Before initiating antiviral therapy
        - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age

Patients with compensated cirrhosis who have any of the following are NOT eligible for simplified treatment:

- Current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 7)
- Prior hepatitis C treatment
- End-stage renal disease (i.e., eGFR less than 30 mL/min/m^2)
- HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

The recommended regimens for genotype 1-6 are glecaprevir (300 mg)/pibrentasvir (120 mg) taken with food for 8 weeks or for genotypes 1, 2, 4, 5, or 6, sofosbuvir (400 mg)/velpatasvir (100 mg) for a duration of 12 weeks (note for sofosbuvir/velpatasvir: patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with sofosbuvir/velpatasvir for a duration of 12 weeks).

Efficacy

Epclusa[1]

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 (SVR12) 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, less than 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 SVR12 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. SVR12 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.

Trial 4062 was on open-label clinical trial that evaluated 12 weeks of treatment with Epclusa in 59 HCV-infected adults with end stage renal disease (ESRD) requiring dialysis. The overall SVR rate was 95%. Of the subjects completing 12 weeks of Epclusa, 1 subject experienced virologic relapse.

The efficacy of Epclusa once daily for 12 weeks was evaluated in an open-label trial (Study 1143) in 173 genotype 1, 2, 3, 4, or 6 HCV treatment-naïve or treatment-experienced pediatric subjects 3 years of age and older without cirrhosis or with compensated cirrhosis.

In patients 12 years to less than 18 years of age (genotypes 1, 2, 3, 4 and 6), the SVR rates were:
- 93% for genotype 1
- 100% for genotypes 2, 3, 4, and 6

In patients 6 years to less than 12 years of age (genotypes 1, 2, 3, and 4) the SVR rates were:
- 93% for genotype 1
- 91% for genotype 3
- 100% for genotypes 2 and 4

In patients 3 years to less than 6 years of age the SVR rates were:
- 83% among all subjects
- 88% for genotype 1
- 50% for genotype 2
- 100% for genotype 3 and 4

Trial 2104 was an open-label clinical trial that evaluated 12 weeks of treatment with Epclusa in 79 HCV-infected treatment-naïve and previously treated adult subjects who had undergone liver transplantation. The overall SVR12 rate was 96%.

Trial 4062 was an open-label clinical trial that evaluated 12 weeks of treatment with Epclusa in 59 HCV-infected adults with end stage renal disease (ESRD) requiring dialysis. The overall SVR rate was 95%.

Harvoni[2]
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[3]
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 patients 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 EDURANCE-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%.

DORA part 2 enrolled patients aged 3 years to less than 12 years and used weight-based dosing of Mavyret. The overall SVR12 rate for the subjects who received the recommended dosage was 98.4%.

Sovaldi[4]
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.

Viekira PAK[5]
Viekira Pak (ombitasvir/paritaprevir/ritonavir co-packaged with dasabuvir) 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-1, SAPPHIRE-II, PEARL-II, PEARL-III, PEARL-IV, TURQUOISE-II, AND TURQUIOISE-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[6]
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[7]
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 m^2) or CKD Stage 5 (eGFR less than 15 mL/min/1.73 m^2), 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[1-7]
- **Epclusa** (sofosbuvir/velpatasvir) has the following contraindication(s):
  - Epclusa and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated
- **Harvoni** (ledipasvir/sofosbuvir) has the following contraindication(s):
  - If used in combination with ribavirin, all contraindications to ribavirin also apply to Harvoni combination therapy
- **Mavyret** (glecaprevir/pibrentasvir) has the following contraindication(s):
  - Patients with severe hepatic impairment (Child-Turcotte-Pugh B or C) or those with any history of prior hepatic decompensation
  - Coadministration with atazanavir or rifampin
- **Sovaldi** (sofosbuvir) has the following contraindication(s):
  - When used in combination with peginterferon alfa/ribavirin or ribavirin alone, all contraindications to peginterferon alfa and/or ribavirin also apply to Sovaldi combination therapy
  - Because ribavirin may cause birth defects and fetal death, Sovaldi in combination with peginterferon alfa and/or ribavirin is contraindicated in pregnant women and men whose female partners are pregnant
- **Viekira PAK** (paritaprevir/ritonavir/ombitasvir + dasabuvir) has the following contraindication(s):

- Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Turcotte-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 is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen

- **Zepatier** (elbasvir/grazoprevir) has the following contraindication(s):
  - Patients with moderate or severe hepatic impairment [decompensated cirrhosis (Child-Turcotte-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

Risk of Hepatitis B infection reactivation with HCV Direct Acting Antivirals[10]
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 an 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 an HCV DAA.

References

1. Epclusa prescribing information. Gilead. April 2022.
2. Harvoni prescribing information. Gilead. March 2020.
3. Mavyret prescribing information. AbbVie. September 2021.
4. Sovaldi prescribing information. Gilead. March 2020.
5. Viekira Pak prescribing information. Abbvie Inc. December 2019.
6. Vosevi prescribing information. Gilead. November 2019.
7. Zepatier prescribing information. Merck. May 2022.
8. AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Testing Hepatitis C. Available at www.hcvguidelines.org.
9. The Centers for Disease Control and Prevention. Viral Hepatitis Statistics and Surveillance. Available at http://www.cdc.gov/hepatitis/statistics.
10. Direct-Acting Antivirals for Hepatitis C: FDA Drug Safety Communication-Risk of Hepatitis B Reactivation. Available at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm523690.htm
11. AASLD/IDSA HCV Guidance: Unique and Key populations – HCV in children. https://www.hcvguidelines.org/unique-populations/children.
12. AASLD-IDSA Hepatitis C Guidance Panel. Hepatitis C Guidance 2019 Update: American Association for the Study of Liver Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Hepatology, Vol. 71, No.2, 2020.

Document History
Original Client Specific review of Client Specific criteria approved by BCBS M Pharmacy Clinical Team (PCT) 09/2014
Initial Review Prime Standard criteria (removed Sovaldi and added Viekira) approved by UM P&T Committee 01/2015
Client Specific Initial Review Prime Standard criteria (removed Sovaldi and added Viekira) approved by BCBS M PCT 01/2015
Client Specific Mid-Year Review Client Specific criteria, added grandfathering, approved by BCBS M PCT 03/2015
Administrative Action (corrected question set) 05/2015

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

TARGET AGENT(S)

Preferred Agent(s)[a,c]	Non-Preferred Agent(s)[c,d]
Genotype 1 **Epclusa®** (sofosbuvir/velpatasvir) **Harvoni®** (ledipasvir/sofosbuvir) **Ledipasvir/Sofosbuvir** **Sofosbuvir/Velpatasvir** **Mavyret®** (glecaprevir/pibrentasvir) **Vosevi®** (sofosbuvir/velpatasvir/voxilaprevir)	**Genotype 1** **Sovaldi®** (sofosbuvir)[b] **Viekira PAK®** (ombitasvir/paritaprevir/ritonavir + dasabuvir) **Zepatier®** (elbasvir/grazoprevir)
Genotype 2 **Epclusa®** (sofosbuvir/velpatasvir) **Sofosbuvir/Velpatasvir** **Mavyret®** (glecaprevir/pibrentasvir) **Vosevi®** (sofosbuvir/velpatasvir/voxilaprevir)	**Genotype 2** **Sovaldi®** (sofosbuvir)[b]
Genotype 3 **Epclusa®** (sofosbuvir/velpatasvir) **Sofosbuvir/Velpatasvir** **Mavyret®** (glecaprevir/pibrentasvir) **Vosevi®** (sofosbuvir/velpatasvir/voxilaprevir)	**Genotype 3** **Sovaldi®** (sofosbuvir)[b]
Genotype 4 **Epclusa®** (sofosbuvir/velpatasvir) **Harvoni®** (ledipasvir/sofosbuvir) **Ledipasvir/Sofosbuvir** **Sofosbuvir/Velpatasvir** **Mavyret®** (glecaprevir/pibrentasvir) **Vosevi®** (sofosbuvir/velpatasvir/voxilaprevir)	**Genotype 4** **Sovaldi®** (sofosbuvir)[b] **Zepatier®** (elbasvir/grazoprevir)
Genotype 5 **Epclusa®** (sofosbuvir/velpatasvir) **Harvoni®** (ledipasvir/sofosbuvir) **Ledipasvir/Sofosbuvir** **Sofosbuvir/Velpatasvir** **Mavyret®** (glecaprevir/pibrentasvir) **Vosevi®** (sofosbuvir/velpatasvir/voxilaprevir)	**Genotype 5**
Genotype 6 **Epclusa®** (sofosbuvir/velpatasvir) **Harvoni®** (ledipasvir/sofosbuvir) **Ledipasvir/Sofosbuvir** **Sofosbuvir/Velpatasvir**	**Genotype 6**

Mavyret® (glecaprevir/pibrentasvir) **Vosevi®** (sofosbuvir/velpatasvir/voxilaprevir)	

a - Preferred agents will require prior authorization. The prior authorization for a specific agent will be based the Food and Drug Administration (FDA) approved product labeling for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs. experienced, previous treatment)
b - Sovaldi is non-preferred for patients without hepatocellular carcinoma.
c – HCV/HIV-1 co-infection, follow recommendations in table above
d – Offer only those preferred agents that are indicated for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)
Epclusa (sofosbuvir/velpatasvir)			
150 mg sofosbuvir/37.5 mg velpatasvir packet with oral pellets	12359902653020	M, N, O, or Y	1 packet
200 mg sofosbuvir/50 mg packet with oral pellets	12359902653030	M, N, O, or Y	1 packet
200 mg sofosbuvir/50 mg velpatasvir tablets	12359902650320	M. N, O, or Y	1 tablet
400 mg sofosbuvir/100 mg velpatasvir tablets	12359902650330	M, N, O, or Y	1 tablet
Harvoni (ledipasvir/sofosbuvir)			
33.75 mg/150 mg packet with oral pellets	12359902403006	M, N, O, or Y	1 packet
45 mg/200 mg tablets	12359902400310	M, N, O, or Y	1 tablet
45 mg/200 mg packet with oral pellets	12359902403010	M, N, O, or Y	1 packet
90 mg ledipasvir/ 400 mg sofosbuvir tablets	12359902400320	M, N, O, or Y	1 tablet
Ledipasvir/sofosbuvir			
90 mg ledipasvir/ 400 mg sofosbuvir tablets	12359902400320	M, N, O, or Y	1 tablet
Mavyret (glecaprevir/pibrentasvir)			
50 mg glecaprevir/20 mg pibrentasvir packets	12359902353020	M, N, O, or Y	5 packets
100 mg glecaprevir/40 mg pibrentasvir tablets	12359902350320	M, N, O, or Y	3 tablets
Sofosbuvir/velpatasvir			
400 mg sofosbuvir/ 100 mg velpatasvir tablets	12359902650330	M, N, O, or Y	1 tablet
Sovaldi (sofosbuvir)			
150 mg packet with oral pellets	12353080003015	M, N, O, or Y	1 packet
200 mg tablets	12353080000310	M, N, O, or Y	1 tablet
200 mg packet with oral pellets	12353080003020	M, N, O, or Y	1 packet
400 mg tablets	12353080000320	M, N, O, or Y	1 tablet
Viekira PAK (ombitasvir/paritaprevir/ritonavir + dasabuvir)			
12.5/75/50 mg ombitasvir/ paritaprevir/ritonavir + 250 mg dasabuvir tablets	1235990460B720	M, N, O, or Y	1 pack (112 tablets)/28 days
Vosevi (sofosbuvir/velpatasvir/voxilaprevir)			
400 mg sofosbuvir/100 mg velpatasvir/100 mg voxilaprevir tablets	12359903800330	M, N, O, or Y	1 tablet
Zepatier (elbasvir/grazoprevir)			
50 mg elbasvir/100 mg grazoprevir tablets	12359902300320	M, N, O, or Y	1 tablet

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Epclusa and Sofosbuvir/Velpatasvir Evaluation

Target Agent(s) 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 in the past 30 days
      OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of hepatitis C genotype 1, 2, 3, 4, 5, or 6
      AND
      ii. 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
         OR
         c. The patient has decompensated cirrhosis
      AND
      iii. If the patient has an FDA approved indication, ONE of the following:
         a. The patient's age is within FDA labeling for the requested indication for the requested agent
         OR
         b. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication
      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. ONE of the following:
         a. 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
         OR
         b. ALL of the following:
            1. The patient is treatment is treatment naïve
            AND
            2. The patient does NOT have cirrhosis or has compensated cirrhosis
            AND
            3. The requested agent is supported in AASLD guidelines for simplified treatment
            AND
            4. The patient meets all of the qualifications for AASLD guidelines simplified treatment (please see Patient Who Qualify for simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment

- Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7)
- Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2)
- HBsAg negative
- NOT currently pregnant
- No known or suspected hepatocellular carcinoma
- No prior liver transplantation

2. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
3. The patient meets all requirements and will use the requested agent in a treatment regimen noted in Table 1 (FDA labeling) or 2 (AASLD/IDSA guidelines for decompensated cirrhosis)
   AND
4. BOTH of the following:
   A. The requested length of therapy does NOT exceed the length of therapy noted in Table 1 (FDA labeling) or 2 (AASLD/IDSA guidelines for decompensated cirrhosis) for the patient's treatment regimen
   AND
   B. ONE of the following:
      i. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
      ii. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following:
         a. The requested agent is Epclusa 200 mg/50 mg packets AND BOTH of the following:
            1. The requested quantity (dose) does NOT exceed 2 packets per day
            AND
            2. The prescriber has provided information supporting why the patient cannot take 1 tablet of the 400 mg/100 mg tablet
         OR
         b. The requested agent is Epclusa 200 mg/50 mg tablet AND BOTH of the following:
            1. The requested quantity (dose) does NOT exceed 2 tablets per day
            AND
            2. The prescriber has provided information supporting why the patient cannot take 1 tablet of the 400 mg/100mg tablet

Length of Approval: Up to the duration of treatment as determined in Tables 1 or 2

Table 1: Epclusa or Sofosbuvir/Velpatasvir Treatment Recommendations based on FDA labeling

Genotype	Patients 3 years of age and older*	Treatment	Duration
1, 2, 3, 4, 5, or 6	Patients without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Epclusa, Sofosbuvir/Velpatasvir	12 weeks
	Patients with decompensated cirrhosis (Child-Turcotte-Pugh B and C)	Epclusa + ribavirin, Sofosbuvir/Velpatasvir + ribavirin	12 weeks

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

Table 2: Epclusa or Sofosbuvir/Velpatasvir Decompensated Cirrhosis Treatment Recommendations based on AASLD/IDSA Guidelines for unique populations

Genotype	Patient Population*	Treatment	Duration
1, 2, 3, 4, 5, or 6	Patients with decompensated cirrhosis (Child-Turcotte-Pugh B and C) who are ribavirin ineligible (i.e., patients with history of intolerance, contraindication, or hypersensitivity to ribavirin)	Epclusa, Sofosbuvir/Velpatasvir	24 weeks
1, 2, 3, 4, 5, or 6	Patients with decompensated cirrhosis (Child-Turcotte-Pugh B and C) in whom prior sofosbuvir- or NS5A inhibitor (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) -based treatment failed	Epclusa with weight-based ribavirin (low initial dose of ribavirin [600 mg] is recommended for patients with Child-Turcotte-Pugh class C cirrhosis), Sofosbuvir/Velpatasvir with weight-based ribavirin (low initial dose of ribavirin [600 mg] is recommended for patients with Child-Turcotte-Pugh class C cirrhosis)	24 weeks

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

Harvoni and Ledipasvir/Sofosbuvir Evaluation

Target Agent(s) 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 in the past 30 days
    OR
    B. The patient is new to therapy and ALL of the below:
        i. The patient has a diagnosis of 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:
            a. The patient is treatment naïve
            OR
            b. The patient was previously treated (i.e., treatment experienced) with peg-interferon and ribavirin with or without an HCV protease inhibitor
            OR
            c. The patient has decompensated cirrhosis
        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. If the patient has an FDA approved indication, ONE of the following:

a. The patient's age is within FDA labeling for the requested indication for the requested agent
OR
b. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication

AND

vii. ONE of the following:
a. 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 **OR**
b. ALL of the following:
1. The patient is treatment is treatment naïve
AND
2. The patient does NOT have cirrhosis or has compensated cirrhosis
AND
3. The requested agent is supported in AASLD guidelines for simplified treatment
AND
4. The patient meets all of the qualifications for AASLD guidelines simplified treatment (please see Patient Who Qualify for simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

2. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
3. The patient meets all requirements and will use the requested agent in a treatment regimen noted in Table 3 (FDA labeling) or 4 (AASLD/IDSA guidelines for decompensated cirrhosis)
AND
4. BOTH of the following:
A. The requested length of therapy does NOT exceed the length of therapy noted in Table 3 (FDA labeling) or 4 (AASLD/IDSA guidelines for decompensated cirrhosis) for the patient's treatment regimen
AND
B. ONE of the following:
i. The requested quantity (dose) does NOT exceed the program quantity limit
OR
ii. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following:
a. The requested agent is Harvoni 45 mg/200 mg oral pellets AND BOTH of the following:
1. The requested quantity (dose) does NOT exceed 2 packets daily

AND

2. The prescriber has provided information stating why the patient cannot take 1 tablet of Harvoni 90 mg/400 mg strength

OR

b. The requested agent is Harvoni 45 mg/200 mg tablet AND BOTH of the following:
   1. The requested quantity (dose) does NOT exceed 2 tablets daily

   AND

   2. 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 or 4

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

Genotype	Patients 3 years of age and older*	Treatment	Treatment Duration
1	Treatment-naïve with initial viral load of less than 6 M IU/mL and without cirrhosis, HIV infection, history of liver transplantation and/or are not black or African-American	Harvoni, Ledipasvir/Sofosbuvir	8 weeks* **NOTE: approve 8 weeks length of therapy ONLY if prescriber is requesting 8 weeks of therapy**
	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Harvoni, Ledipasvir/Sofosbuvir	12 weeks
	Treatment-experienced (i.e., patients who have failed therapy with either peg-interferon + ribavirin ± an HCV protease inhibitor [e.g., boceprevir, paritaprevir, simeprevir, telaprevir]) without cirrhosis	Harvoni, Ledipasvir/Sofosbuvir	12 weeks
	Treatment-experienced (i.e., patients who have failed therapy with either peg-interferon + ribavirin ± an HCV protease inhibitor [e.g., boceprevir, paritaprevir, simeprevir, telaprevir]) with compensated cirrhosis (Child-Turcotte-Pugh A) and eligible for ribavirin	Harvoni + ribavirin, Ledipasvir/Sofosbuvir + ribavirin	12 weeks
	Treatment-experienced (i.e., patients who have failed therapy with either peg-interferon + ribavirin ± an HCV protease inhibitor [e.g., boceprevir, paritaprevir, simeprevir, telaprevir]) with compensated cirrhosis (Child-Turcotte-Pugh A) and ineligible for ribavirin (i.e., patients with a history of	Harvoni, Ledipasvir/Sofosbuvir	24 weeks

	intolerance, contraindication, or hypersensitivity to ribavirin)		
	Treatment-naïve and treatment-experienced (i.e., patients who have failed therapy with either peg-interferon + ribavirin ± an HCV protease inhibitor [e.g., boceprevir, paritaprevir, simeprevir, telaprevir]) with decompensated cirrhosis (Child-Turcotte-Pugh B or C)	Harvoni + ribavirin, Ledipasvir/Sofosbuvir + ribavirin	12 weeks
1 or 4	Treatment-naïve and treatment-experienced (i.e., patients who have failed therapy with either peg-interferon + ribavirin ± an HCV protease inhibitor [e.g., boceprevir, paritaprevir, simeprevir, telaprevir]) liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Turcotte-Pugh A)	Harvoni + ribavirin, Ledipasvir/Sofosbuvir + ribavirin	12 weeks
4, 5, or 6	Treatment-naïve and treatment-experienced (i.e., patients who have failed therapy with either peg-interferon + ribavirin ± an HCV protease inhibitor [e.g., boceprevir, paritaprevir, simeprevir, telaprevir]) without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Harvoni, Ledipasvir/Sofosbuvir	12 weeks

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

Table 4: Harvoni or Ledipasvir/Sofosbuvir Decompensated Cirrhosis Treatment Recommendations based on AASLD Guidelines for unique populations

Genotype	Patients 3 years of age and older*	Treatment	Duration
1, 4, 5, or 6	Patients with decompensated cirrhosis (Child-Turcotte-Pugh B or C) AND are ribavirin ineligible (i.e., patients with history of intolerance, contraindication, or hypersensitivity to ribavirin)	Harvoni, Ledipasvir/Sofosbuvir	24 weeks
1, 4, 5, or 6	Patients with decompensated cirrhosis (Child-Turcotte-Pugh B or C) previously treated with sofosbuvir-based treatment failure	Harvoni + low initial dose of ribavirin (600 mg); increase as tolerated, Ledipasvir/Sofosbuvir + low initial dose of ribavirin (600 mg); increase as tolerated	24 weeks

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

Mavyret Evaluation

Target Agent(s) 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 in the past 30 days
OR
B. The patient is new to therapy and ALL of the below:
i. The patient has a diagnosis of hepatitis C genotype 1, 2, 3, 4, 5, or 6
AND
ii. If the patient has an FDA approved indication, ONE of the following:
a. The patient's age is within FDA labeling for the requested indication for the requested agent
OR
b. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication
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. ONE of the following:
a. 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 **OR**
b. ALL of the following:
1. The patient is treatment naïve
AND
2. The patient does NOT have cirrhosis or has compensated cirrhosis
AND
3. The requested agent is supported in AASLD guidelines for simplified treatment
AND
4. The patient meets all of the qualifications for AASLD guidelines simplified treatment (please see Patients Who Qualify for Simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

vi. The patient has not been previously treated with the requested agent
AND
2. The patient does NOT have any FDA labeled contraindications to the requested agent
AND

3. The patient meets all requirements and will use the requested agent will in a treatment regimen noted in Table 5 (FDA labeling)
   AND
4. BOTH of the following:
   A. The requested length of therapy does NOT exceed the length of therapy noted in Table 5 (FDA labeling) for the patient's treatment regimen
   AND
   B. ONE of the following:
      i. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
      ii. The requested quantity (dose) exceeds the program quantity limit AND ALL of the following:
         a. The requested agent is Mavyret 50 mg/20 mg packets
         AND
         b. The requested quantity (dose) does NOT exceed 6 packets per day
         AND
         c. The prescriber has provided information supporting why the patient cannot take 3 tablets of the 100 mg/40 mg tablet

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

Table 5: **Mavyret Treatment Recommendations based on FDA labeling**

Genotype	Patient Population - adults and pediatric patients 3 years of age and older*†	Treatment	Duration	
			No Cirrhosis	Compensated Cirrhosis (Child-Turcotte-Pugh A)
1, 2, 3, 4, 5, or 6	Liver or kidney transplant recipients	Mavyret	12 weeks	12 weeks
1	Liver or kidney transplant recipients who are treatment experienced with an NS5A inhibitor (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) but without prior treatment with an NS3/4A protease inhibitor (PI)	Mavyret	16 weeks	16 weeks
3	Liver or kidney transplant recipients who are treatment experienced with PRS (i.e., 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)	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 (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir,	Mavyret	16 weeks	16 weeks

	velpatasvir) but without prior treatment with an NS3/4A protease inhibitor (PI)			
1	Treatment experienced with an NS3/4A protease inhibitor (e.g., simeprevir, boceprevir, telaprevir) but without prior treatment with an NS5A inhibitor	Mavyret	12 weeks	12 weeks
1, 2, 4, 5, or 6	Treatment experienced with PRS (i.e., 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)	Mavyret	8 weeks	12 weeks
3	Treatment experienced with PRS (i.e., 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)	Mavyret	16 weeks	16 weeks

* HCV/HIV-1 co-infection, follow recommendation in table above
† Patients with any degree of kidney impairment (including those on hemodialysis), follow recommendation in table above

Sovaldi Evaluation
Target Agent(s) 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 in the past 30 days
    OR
    B. The patient is new to therapy and ALL of the below:
        i. ONE of the following:
            a. The patient is a pediatric patient with a diagnosis of hepatocellular carcinoma secondary to chronic hepatitis C genotype 2 or 3 AND if the patient has an FDA approved indication, ONE of the following:
                1. The patient's age is within FDA labeling for the requested agent for the requested indication
                OR
                2. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication

            OR

            b. The patient is a pediatric patient with a diagnosis of hepatitis C genotype 2 or 3 AND ALL of the following:
                1. If the patient has an FDA approved indication, ONE of the following:
                    A. The patient's age is within FDA labeling for the requested agent for the requested indication
                    OR
                    B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication

AND

2. ONE of the following:
    A. The patient has an intolerance or hypersensitivity to BOTH Epclusa and Mavyret
    OR
    B. The patient has an FDA labeled contraindication to BOTH Epclusa and Mavyret
    OR
    C. The prescriber has provided information supporting the use of the requested agent over BOTH Epclusa and Mavyret (e.g., the patient is currently taking the requested agent)
    OR
    D. The patient is currently being treated with the requested agent as indicated by ALL of the following:
        i. A statement by the prescriber that the patient is currently taking the requested agent
        AND
        ii. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
        AND
        iii. The prescriber states that a change in therapy is expected to be ineffective or cause harm
    OR
    E. The prescriber has provided documentation that BOTH Epclusa and Mavyret 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

AND

3. 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

OR

c. The patient is an adult and has a diagnosis of hepatocellular carcinoma secondary to chronic hepatitis C genotype 1, 2, 3, or 4
OR
d. The patient is an adult with a diagnosis of hepatitis C genotype 1, 2, 3, or 4 AND BOTH of the following:
    1. 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

    2. If the client has preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment), then ONE of the following:
        A. Information has been provided that indicates the patient has been treated with the requested non-preferred agent in the past 30 days
        OR

B. The patient has an intolerance or hypersensitivity to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
OR
C. The patient has an FDA labeled contraindication to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
OR
D. The prescriber has provided clinical information supporting the use of the non-preferred agent over the preferred agent(s)
OR
E. The patient is currently being treated with the requested agent as indicated by ALL of the following:
    i. A statement by the prescriber that the patient is currently taking the requested agent
    AND
    ii. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
    AND
    iii. The prescriber states that a change in therapy is expected to be ineffective or cause harm
OR
F. The prescriber has provided documentation that ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment) 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

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. ONE of the following:
    a. 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
    OR
    b. ALL of the following:
        1. The patient is treatment naïve
        AND
        2. The patient does NOT have cirrhosis or has compensated cirrhosis
        AND
        3. The requested agent is supported in AASLD guidelines for simplified treatment
        AND

4. The patient meets all the qualifications for AASLD guidelines simplified treatment (please see Patients Who Qualify for Simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

2. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
3. The patient meets all requirements and will use the requested agent in a treatment regimen noted in Table 6 or 7 (FDA labeling)
   AND
4. BOTH of the following:
   A. The requested length of therapy does NOT exceed the length of therapy noted in Table 6 or 7 (FDA labeling) for the patient's treatment regimen
   AND
   B. ONE of the following:
      i. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
      ii. The requested agent is Sovaldi 200 mg oral pellets AND BOTH of the following:
         a. The requested quantity (dose) does NOT exceed 2 packets daily
         AND
         b. The prescriber has provided information stating why the patient cannot take 1 tablet of Sovaldi 400 mg strength
      OR
      iii. The requested agent is Sovaldi 200 mg tablets AND BOTH of the following:
         a. The requested quantity (dose) does NOT exceed 2 tablets daily
         AND
         b. 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 6 or 7

Table 6: Sovaldi Treatment Recommendations in Adult Patients with Genotype 1, 2, 3, or 4 Based on FDA Labeling

Genotype	Patient population*	Treatment	Duration
1 or 4	Treatment naïve without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Sovaldi + Peg-interferon alfa + ribavirin	12 weeks

1	Treatment naïve without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A) and are interferon ineligible 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)	Sovaldi + ribavirin	24 weeks
2	Treatment naïve or treatment experienced (i.e., patients who have failed an interferon based regimen with or without ribavirin) without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Sovaldi + ribavirin	12 weeks
3	Treatment naïve or treatment experienced (i.e., patients who have failed an interferon based regimen with or without ribavirin) without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Sovaldi + ribavirin	24 weeks
1-4	With hepatocellular carcinoma awaiting liver transplantation	Sovaldi + ribavirin	Up to 48 weeks

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

Table 7: Sovaldi and Ribavirin with or without Peg-interferon Treatment Recommendations for Pediatric Patients 3 Years of Age and Older Based on FDA Labeling

Genotype	Patient population*	Treatment	Duration
2	Treatment-naïve and treatment experienced (i.e., patients who have failed an interferon-based regimen with or without ribavirin) without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Sovaldi + ribavirin	12 weeks
3	Treatment-naïve and treatment experienced (i.e., patients who have failed an interferon-based regimen with or without ribavirin) without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Sovaldi + ribavirin	24 weeks
2 or 3	Pediatric patients with hepatocellular carcinoma awaiting liver transplantation	Sovaldi + ribavirin	48 weeks

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

Viekira Pak Evaluation

Target Agent(s) 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 in the past 30 days
    OR
    B. The patient is new to therapy and ALL of the below:
        i. The patient has a diagnosis of hepatitis C genotype 1
        AND
        ii. The prescriber has provided the patient's subtype
        AND
        iii. 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
        iv. If the patient has an FDA approved indication, ONE of the following:
            a. The patient's age is within FDA labeling for the requested indication for the requested agent
            OR
            b. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication
        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. ONE of the following:
            a. 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

OR

b. ALL of the following:
    1. The patient is treatment naïve
       AND
    2. The patient does NOT have cirrhosis or has compensated cirrhosis
       AND
    3. The requested agent is supported in AASLD guidelines for simplified treatment
       AND
    4. The patient meets all the qualifications for AASLD guidelines simplified treatment (please see Patients Who Qualify for Simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

viii. If the client has preferred agents for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment), then ONE of the following:
    a. Information has been provided that indicates the patient has been treated with the requested non-preferred agent in the past 30 days
       OR
    b. The patient has an intolerance or hypersensitivity to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
       OR
    c. The patient has an FDA labeled contraindication to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
       OR
    d. The prescriber has provided clinical information supporting the use of the non-preferred agent over the preferred agent(s)
       OR
    e. The patient is currently being treated with the requested agent as indicated by ALL of the following:
        1. A statement by the prescriber that the patient is currently taking the requested agent
           AND
        2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
           AND
        3. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

f. The prescriber has provided documentation that ALL preferred agent(s) for the patient's specific factors (e.g., age and/or weight, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment) 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

AND

2. The patient does NOT have any FDA contraindications to the requested agent
   AND
3. The patient meets all requirements and will use the requested agent will be used in a treatment regimen noted in Table 8 (FDA labeling)
   AND
4. BOTH of the following:
   A. The requested length of therapy does NOT exceed the length of therapy noted in Table 8 (FDA labeling) for the patient's treatment regimen
   AND
   B. The requested quantity (dose) does NOT exceed the program quantity limit

Length of Approval: Up to the duration as determined in Table 8

Table 8: Viekira PAK Treatment Recommendations based on FDA labeling

Genotype	Patient Population*	Treatment	Duration
1a	Without cirrhosis	Viekira PAK + ribavirin	12 weeks
	With compensated cirrhosis	Viekira PAK + ribavirin	24 weeks
1b	With or without compensated cirrhosis	Viekira PAK	12 weeks
1a or 1b	Post liver transplant with normal hepatic function (i.e. Metavir less than or equal to 2)	Viekira PAK + ribavirin	24 weeks

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

Vosevi Evaluation

Target Agent(s) 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 in the past 30 days
   OR
   B. The patient is new to therapy and ALL of the below:
      i. The patient has a diagnosis of 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. If the patient has an FDA approved indication, ONE of the following:
         a. The patient's age is within FDA labeling for the requested indication for the requested agent
         OR

b. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication

AND

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

AND

vii. 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

viii. ONE of the following:

a. 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

OR

b. ALL of the following:

1. The patient is treatment naïve

AND

2. The patient does NOT have cirrhosis or has compensated cirrhosis

AND

3. The requested agent is supported in AASLD guidelines for simplified treatment

AND

4. The patient meets all the qualifications for AASLD guidelines simplified treatment (please see Patients Who Qualify for Simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

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

AND

3. The patient meets all requirements and will use the requested agent in a treatment regimen noted in Table 9

AND

4. BOTH of the following:

A. The requested length of therapy does NOT exceed the length of therapy noted in Table 9 (FDA labeling) for the patient's regimen

AND

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

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

Table 9: **Vosevi Treatment Recommendations based on FDA labeling**

Genotype	Patient Population*	Patients Previously Treated with an HCV Regimen Containing:	Treatment Duration
1,2,3,4,5, or 6	Without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	An NS5A inhibitor (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir)	12 weeks
1a or 3	Without cirrhosis or with compensated cirrhosis (Child-Turcotte-Pugh A)	Sofosbuvir without an NS5A inhibitor†	12 weeks

* – HCV/HIV-1 co-infection, follow recommendation in table above
† - Sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (simeprevir)

Zepatier Evaluation

Target Agent(s) 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 in the past 30 days
    OR
    B. The patient is new to therapy and ALL of the below:
        i. The patient has a diagnosis of hepatitis C genotype 1 or 4
        AND
        ii. 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
        iii. 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
        iv. If the patient has an FDA approved indication, ONE of the following:
            a. The patient's age is within FDA labeling for the requested indication for the requested agent
            OR
            b. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication
        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. ONE of the following:
            a. 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
            OR
            b. ALL of the following:

1. The patient is treatment naïve
   AND
2. The patient does NOT have cirrhosis or has compensated cirrhosis
   AND
3. The requested agent is supported in AASLD guidelines for simplified treatment
   AND
4. The patient meets all the qualifications for AASLD guidelines simplified treatment (please see Patients Who Qualify for Simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

viii. If the client has preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment), then ONE of the following:
   a. Information has been provided indicating that the patient has been treated with the requested non-preferred agent in the past 30 days
      OR
   b. The patient has an intolerance or hypersensitivity to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
      OR
   c. The patient has an FDA labeled contraindication to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
      OR
   d. The prescriber has provided clinical information supporting the use of the requested non-preferred agent over the preferred agent(s)
      OR
   e. The patient is currently being treated with the requested agent as indicated by ALL of the following:
      1. A statement by the prescriber that the patient is currently taking the requested agent
         AND
      2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
         AND
      3. The prescriber states that a change in therapy is expected to be ineffective or cause harm

      OR

f. The prescriber has provided documentation that ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment) 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

AND

2. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
3. The patient meets all requirements and will use the requested agent in a treatment regimen noted in Table 10 (FDA labeling)
   AND
4. BOTH of the following:
   A. The requested length of therapy does NOT exceed the length of therapy noted in Table 10 (FDA labeling) for the patient's treatment regimen
   AND
   B. The requested quantity (dose) does NOT exceed the program quantity limit

Length of Approval: Up to the duration of treatment as determined in Table 10

Table 10: Zepatier Treatment Recommendations based on FDA labeling

Genotype	Patient Population*	Treatment	Duration
1a	Treatment-naïve or PegIFN/RBV-experienced without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	Zepatier	12 weeks
	Treatment-naïve or PegIFN/RBV-experienced with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	Zepatier + ribavirin	16 weeks
1b	Treatment-naïve or PegIFN/RBV-experienced	Zepatier	12 weeks
1a or 1b	PegIFN/RBV/protease inhibitor-experienced	Zepatier + ribavirin	12 weeks
4	Treatment-naive	Zepatier	12 weeks
	PegIFN/RBV-experienced	Zepatier + ribavirin	16 weeks

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

New to Market Hepatitis C Agents Evaluation

Target Agent(s) 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 in the past 30 days
   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 the patient has an FDA approved indication, ONE of the following:
         a. The patient's age is within FDA labeling for the requested indication for the requested agent

OR

b. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication

AND

iv. 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:
   a. The prescriber has screened the patient for current or prior HBV
      AND
   b. 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

v. ONE of the following:
   a. 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
      OR
   b. ALL of the following:
      1. The patient is treatment naïve
         AND
      2. The patient does NOT have cirrhosis or has compensated cirrhosis
         AND
      3. The requested agent is supported in AASLD guidelines for simplified treatment
         AND
      4. The patient meets all the qualifications for AASLD guidelines simplified treatment (please see Patients Who Qualify for Simplified Treatment tables below)

AND

Patients Without Cirrhosis Who Qualify for Simplified Treatment
• Hepatitis B surface antigen (HBsAg) negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation
Patients With Compensated Cirrhosis Who Qualify for Simplified Treatment
• Patient has NOT had current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score greater than or equal to 7 (ascites, hepatic encephalopathy, total bilirubin greater than 2.0 mg/dL, albumin less than or equal to 3.5 g/dL, or INR greater than or equal to 1.7) • Does NOT have end-stage renal disease (i.e., eGFR less than 30 mL/min/m^2) • HBsAg negative • NOT currently pregnant • No known or suspected hepatocellular carcinoma • No prior liver transplantation

vi. If the client has preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment), then ONE of the following:
   a. The requested agent is a preferred agent for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
      OR
   b. Information has been provided indicating that the patient has been treated with the requested non-preferred agent in the past 30 days
      OR

c. The patient has an intolerance or hypersensitivity to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
OR
d. The patient has an FDA labeled contraindication to ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment)
OR
e. The prescriber has provided clinical information supporting the use of the non-preferred agent over the preferred agent(s)
OR
f. The patient is currently being treated with the requested agent as indicated by ALL of the following:
    1. A statement by the prescriber that the patient is currently taking the requested agent
    AND
    2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
    AND
    3. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR
g. The prescriber has provided documentation that ALL preferred agent(s) for the patient's specific factors (e.g., age, genotype, cirrhosis status, treatment naïve vs treatment experienced, previous treatment) 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

AND

2. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
3. The patient meets all requirements and will use the requested agent in a treatment regimen noted in Table 11 (FDA labeling)
AND
4. BOTH of the following:
    A. The requested length of therapy does NOT exceed the length of therapy noted in Table 11 (FDA labeling) for the patient's treatment regimen
    AND
    B. ONE of the following:
        i. The requested quantity (dose) does NOT exceed the program quantity limit
        OR
        ii. BOTH of the following:
            a. The requested quantity (dose) is greater than the program quantity limit
            AND
            b. 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 11

Table 11: Treatment Recommendations based on FDA labeling

Agent(s)	FDA approved indication(s)	Genotype	Treatment Regimen	FDA labeled	Duration

				dose	
TBD	TBD	TBD	TBD	TBD	TBD