

## Medical Policy



An independent licensee of the  
Blue Cross Blue Shield Association

### **Title: Hepatitis C Second Generation Antivirals – Through Preferred Agent(s)**

*See also:*

- *Hepatitis B / Hepatitis C Peg-interferon*
- *Hepatitis C First Generation Agents - Through Preferred Agent(s)*

➤ **Prime Therapeutics will review Prior Authorization requests**

**Prior Authorization Form:**

<http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6349KS-HEPC.pdf>

**Link to Drug List (Formulary):**

<https://www.bcbsks.com/drugs/>

#### **Professional**

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#### **Institutional**

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**State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact [Blue Cross and Blue Shield of Kansas Customer Service](#).**

**The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.**

**The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.**

**If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.**

**DESCRIPTION**

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. 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 non-preferred agent over the preferred agent.

**Target Agent(s)****Preferred Agents**

- **Epclusa**<sup>®</sup> (sofosbuvir/velpatasvir) (co-preferred for genotype 1, 2, 3, 4, 5, and 6)
- **Harvoni**<sup>®</sup> (ledipasvir / sofosbuvir) (co-preferred for genotype 1, 4, 5, and 6)
- **Ledipasvir/Sofosbuvir**
- **Mavyret**<sup>®</sup> (glecaprevir/pibrentasvir) (co-preferred for genotype 1, 2, 3, 4, 5, and 6)
- **Sofosbuvir/Velpatasvir**
- **Vosevi**<sup>®</sup> (sofosbuvir / velpatasvir / voxilaprevir) (co-preferred for genotype 1, 2, 3, 4, 5, and 6)

**Non-Preferred Agent(s)**

<b>Requested agent/regimen</b>	<b>Genotype</b>	<b>Preferred agent(s)*</b>
<b>Technivie</b> <sup>™</sup> (ombitasvir/ paritaprevir/ritonavir)	4	Epclusa Harvoni Mavyret Vosevi
<b>Viekira PAK</b> <sup>™</sup> (ombitasvir/paritaprevir/ritonavir + dasabuvir)	1	Epclusa Harvoni Mavyret Vosevi
<b>Viekira XR</b> <sup>™</sup> (dasabuvir/ombitasvir/paritaprevir/ritonavir)		
<b>Zepatier</b> (elbasvir/grazoprevir)	1 or 4 without renal impairment	Epclusa Harvoni Mavyret Vosevi
	1 or 4 with renal impairment	Mavyret

\* 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 and/or clinical guidelines for the patient's specific factors (e.g. genotype, cirrhosis status, renal function, treatment naïve vs. experienced, previous treatment etc)

**FDA Approved Indications and Dosage** <sup>1,2,3,4,7,8,10,11</sup>

<b>Medication</b>	<b>Indications</b>	<b>Dose and Interval</b>
<b>Epclusa</b> (sofosbuvir/ velpatasvir)	<ul style="list-style-type: none"> <li>▪ Treatment of adult patient with chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection:               <ul style="list-style-type: none"> <li>-Without cirrhosis or with compensated cirrhosis</li> <li>-With decompensated cirrhosis in combination with ribavirin</li> </ul> </li> </ul>	1 tablet orally once daily containing 400 mg of sofosbuvir and 100 mg of velpatasvir for 12 weeks
<b>Harvoni</b> (ledipasvir- sofosbuvir)	<ul style="list-style-type: none"> <li>▪ Treatment of chronic hepatitis C:               <ul style="list-style-type: none"> <li>-For adult patients with genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis</li> <li>-For adult patients with genotype 1 infection with decompensated cirrhosis in combination with ribavirin</li> <li>-For adult patients with genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis in combination with ribavirin</li> <li>-For 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</li> </ul> </li> </ul>	1 tablet orally once daily containing 90 mg of ledipasvir and 400 mg of sofosbuvir. Length of therapy is dependent on genotype, patient treatment experience, and patient cirrhosis status.
<b>Mavyret</b> (glecaprevir/ pibrentasvir)	<ul style="list-style-type: none"> <li>▪ Treatment of adult patients within chronic hepatitis C who have               <ul style="list-style-type: none"> <li>-Genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child Pugh A)</li> <li>-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</li> </ul> </li> </ul>	3 tablets orally once daily with food. Length of therapy is dependent on genotype, patient treatment experience, and patient cirrhosis status
<b>Technivie</b> (ombitasvir/ paritaprevir/ ritonavir)	<ul style="list-style-type: none"> <li>▪ Treatment of chronic hepatitis C genotype 4:               <ul style="list-style-type: none"> <li>-In combination with ribavirin for patients without cirrhosis or with compensated cirrhosis</li> <li>-Without ribavirin for treatment-naïve patients without cirrhosis who cannot take or tolerate ribavirin</li> </ul> </li> </ul>	Two tablets orally once daily (in the morning) with a meal for 12 weeks
<b>Viekira Pak</b> (ombitasvir paritaprevir/ ritonavir/ co-packaged with dasabuvir)	<ul style="list-style-type: none"> <li>▪ Treatment of adult patients, with chronic hepatitis C virus who have:               <ul style="list-style-type: none"> <li>-Genotype 1b without cirrhosis or with compensated cirrhosis</li> <li>-Genotype 1a without cirrhosis or with compensated cirrhosis used in combination with ribavirin</li> </ul> </li> </ul>	Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets orally once daily (in the morning) and one dasabuvir 250 mg tablet twice daily (morning and evening) with a meal. Length of therapy is dependent on genotype and patient cirrhosis status
<b>Viekira XR</b> (dasabuvir/ ombitasvir/ paritaprevir/ ritonavir)	<ul style="list-style-type: none"> <li>▪ Treatment of adult patients with chronic hepatitis C virus who have:               <ul style="list-style-type: none"> <li>-Genotype 1b without cirrhosis or with compensated cirrhosis</li> <li>-Genotype 1a without cirrhosis or with compensated cirrhosis used in combination with ribavirin</li> </ul> </li> </ul>	3 tablets taken orally once daily with a meal. Length of therapy is dependent on genotype and patient cirrhosis status

Medication	Indications	Dose and Interval
<b>Vosevi</b> (sofosbuvir/ velpatasvir/ voxilaprevir)	<ul style="list-style-type: none"> <li>▪ Treatment of adult patients with HCV infection without cirrhosis or compensated cirrhosis (Child-Pugh A) who have:               <ul style="list-style-type: none"> <li>-Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor</li> <li>-Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor</li> </ul> </li> </ul>	1 tablet taken orally once daily with food for 12 weeks
<b>Zepatier</b> (elbasvir/ grazoprevir)	<ul style="list-style-type: none"> <li>▪ Treatment, with or without ribavirin, of chronic hepatitis C genotype 1 or 4 infection</li> </ul>	1 tablet (50 mg elbasvir and 100 mg grazoprevir) taken orally once daily for up to 16 weeks

## **POLICY**

### **Prior Authorization Criteria for Approval**

#### **Epclusa and Sofosbuvir/Velpatasvir Evaluation**

**Epclusa** or **Sofosbuvir/Velpatasvir** 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**
3. 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**
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 1 (FDA labeling)

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

**Table 1: Eplclusa Treatment Recommendations based on FDA labeling**

Genotype	Patient population*	Treatment	Duration
1, 2, 3, 4, 5, or 6	Patients without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Eplclusa	12 weeks
	Patients with decompensated cirrhosis (Child-Pugh B and C)	Eplclusa + ribavirin	12 weeks

\* HCV/HIV-1 co-infection: For patients with HCV/HIV-1 co-infection, follow the Eplclusa dosage recommendations in the table above

### Harvoni and Ledipavir/Sofosbuvir Evaluation

**Harvoni** or **Ledipavir/Sofosbuvir** 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**
4. 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**
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 patient does not have any FDA labeled contraindications to the requested agent  
**AND**
7. 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  
**AND**
8. The dose is within the FDA labeled dose  
**AND**

9. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype see as noted in Table 2 and 3 (FDA labeling)

**Length of Approval:** Up to the duration of treatment as determined in Tables 2 and/or 3.

**Table 2: Harvoni Treatment Recommendations based on FDA Labeling**

Genotype	Adult Patient Population <sup>^</sup>	Treatment	Treatment Duration
1	Treatment-naïve with initial viral load of <6 M IU/mL and without cirrhosis, HIV infection, history of liver transplantation and/or are not black or African-American	Harvoni	8 weeks*
	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks
	Treatment-experienced** without cirrhosis	Harvoni	12 weeks
	Treatment-experienced** with compensated cirrhosis (Child-Pugh A) and eligible for ribavirin	Harvoni + ribavirin	12 weeks <sup>†</sup>
	Treatment-experienced** with compensated cirrhosis (Child-Pugh A) and ineligible for ribavirin <sup>‡</sup>	Harvoni	24 weeks
	Treatment-naïve and treatment-experienced** with decompensated cirrhosis (Child-Pugh B or C)	Harvoni + ribavirin	12 weeks
1 or 4	Treatment-naïve and treatment-experienced** liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)	Harvoni + ribavirin	12 weeks
4, 5, or 6	Treatment-naïve and treatment-experienced** without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks

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

Genotype	Pediatric Patients ≥ 12 years of Age or Weighing at Least 35 Kg <sup>^</sup>	Treatment	Treatment Duration
1	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks
	Treatment-experienced <sup>‡</sup> without cirrhosis	Harvoni	12 weeks
	Treatment-experienced <sup>‡</sup> with compensated cirrhosis (Child-Pugh A)	Harvoni	24 weeks
4, 5, or 6	Treatment-naïve and treatment experienced <sup>‡</sup> , without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks

<sup>^</sup>HCV/HIV co-infected patients: Follow the dosage recommendation in the table above unless otherwise noted.

\*8 weeks may be considered in treatment naïve 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 8 weeks of therapy is required.

\*\*Treatment-experienced - patients who have failed therapy with either peginterferon + ribavirin or an HCV protease inhibitor + peginterferon + ribavirin.

<sup>†</sup> 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.

<sup>‡</sup>Ribavirin ineligible - patients with history of intolerance, contraindication, or hypersensitivity to ribavirin

<sup>‡</sup>Treatment-experienced patients who have failed an interferon based regimen with or without ribavirin

## Mavyret Evaluation

**Mavyret** 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**
3. 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**
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. The patient has not been previously treated with the requested agent  
**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 4 (FDA labeling)

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

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

Genotype	Patient Population*	Treatment	Treatment Duration	
			No Cirrhosis	Compensated Cirrhosis (Child-Pugh A)
1, 2, 3, 4, 5, or 6	Treatment naïve	Mavyret	8 weeks	12 weeks
1	Treatment experienced with an NS5A inhibitor <sup>1</sup> but without prior treatment with an NS3/4A protease inhibitor (PI)	Mavyret	16 weeks	16 weeks
1	Treatment experienced with an NS3/4A protease inhibitor <sup>2</sup> but without prior treatment with an NS5A inhibitor	Mavyret	12 weeks	12 weeks
1, 2, 4, 5, or 6	Treatment experienced with PRS <sup>3</sup>	Mavyret	8 weeks	12 weeks
3	Treatment experienced with PRS <sup>3</sup>	Mavyret	16 weeks	16 weeks

\*Follow the dosage recommendations above for HCV/HIV co infected patient and in patients with any degree of kidney impairment (including those on hemodialysis)

1. Examples of HCV NS5A inhibitors include daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir.

2. Examples of NS3/4A protease inhibitors include simeprevir, boceprevir, telaprevir

3. PRS=Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor.

### Technivie Evaluation

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

1. The patient has a diagnosis of chronic hepatitis C, genotype 4  
**AND**
2. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection  
**AND**
3. 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**
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 contraindication 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  
**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 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**

Patient population	Treatment	Treatment Duration
Genotype 4 without cirrhosis and the patient ribavirin eligible	Technivie + ribavirin	12 weeks
Genotype 4, treatment naïve, without cirrhosis and the patient ribavirin ineligible*	Technivie	12 weeks
Genotype 4 with compensated cirrhosis	Technivie + ribavirin	12 weeks

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



### Viekira Pak and Viekira XR Evaluation

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

1. The patient has a diagnosis of 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**
4. 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**
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 patient does not have any FDA contraindications to the requested agent  
**AND**
7. 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**
8. The dose is within the FDA labeled dose  
**AND**
9. 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**

Patient Population	Treatment*	Treatment Duration
Genotype 1a, without cirrhosis	Viekira PAK + ribavirin OR Viekira XR + ribavirin	12 weeks
Genotype 1a, with compensated cirrhosis	Viekira PAK + ribavirin OR Viekira XR + ribavirin	24 weeks**
Genotype 1b, with or without compensated cirrhosis	Viekira PAK OR Viekira XR	12 weeks

Patient Population	Treatment*	Treatment Duration
Genotype 1a or 1b, post liver transplant with normal hepatic function (i.e. Metavir $\leq 2$ )	Viekira PAK + ribavirin OR Viekira XR + ribavirin	24 weeks

\*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.

### Vosevi Evaluation

**Vosevi** 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. If genotype 1, 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**
4. 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**
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 patient does not have any FDA labeled contraindications to the requested agent  
**AND**
7. BOTH of the following:
  - A. The patient is not treatment naïve  
**AND**
  - B. The patient has not been previously treated with the requested agent  
**AND**
8. The dose is within the FDA labeled dose  
**AND**
9. 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: Vosevi Treatment Recommendations based on FDA labeling**

<b>Patient Population</b>	<b>Patients Previously Treated with an HCV Regimen Containing:</b>	<b>Treatment Duration</b>
Genotype 1,2,3,4,5, or 6 without cirrhosis or with compensated cirrhosis (Child Pugh A)	An NS5A inhibitor <sup>a</sup>	12 weeks
Genotype 1a or 3 without cirrhosis or with compensated cirrhosis (Child Pugh A)	Sofosbuvir without an NS5A inhibitor <sup>b</sup>	12 weeks

a Examples of HCV NS5A inhibitors include daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir

b Sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (simeprevir)

### Zepatier Evaluation

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

1. The patient has a diagnosis of 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**
4. 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**
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 patient does not have any FDA labeled contraindications to the requested agent  
**AND**
7. 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**
8. The dose is within the FDA labeled dose  
**AND**

9. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype as noted in Table 8 (FDA labeling)

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

**Table 8: Zepatier Treatment Recommendations based on FDA labeling**

Patient Population <sup>^</sup> <sup>£</sup>	Treatment	Duration
<b>Genotype 1a:</b> Treatment-naïve or PegIFN/RBV-experienced <u>without</u> baseline NS5A polymorphisms <sup>†</sup>	Zepatier	12 weeks
<b>Genotype 1a:</b> Treatment-naïve or PegIFN/RBV-experienced <u>with</u> baseline NS5A polymorphisms <sup>†</sup>	Zepatier + ribavirin	16 weeks
<b>Genotype 1b:</b> Treatment-naïve or PegIFN/RBV-experienced	Zepatier	12 weeks
<b>Genotype 1a or 1b:</b> PegIFN/RBV/protease inhibitor-experienced	Zepatier + ribavirin	12 weeks
<b>Genotype 4:</b> Treatment-naïve	Zepatier	12 weeks
<b>Genotype 4:</b> PegIFN/RBV-experienced	Zepatier + ribavirin	16 weeks

<sup>†</sup>Polymorphisms at amino acid positions 28, 30, 31, or 93

<sup>^</sup>Genotype 1a: Testing for the presence of virus with NS5A resistance-associated polymorphisms is recommended.

<sup>£</sup>HCV/HIV co-infection and/or cirrhosis: follow dosage recommendations in the table above

### New To Market Chronic Hepatitis C Agents Evaluation

**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. BOTH of the following:
    - i. The prescriber has screened the patient for current or prior HBV  
**AND**
    - ii. 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**
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 9 (FDA labeling)

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

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

Agent(s)	FDA approved indication(s)	Geno-type	Treat-ment	FDA Labeled dose	Treatment Duration

### Non-Preferred Agents Evaluation

- A. **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. The prescriber has submitted documentation in support of the use of the non-preferred agent over the preferred agent(s)

Agent(s)	Contraindication(s)
<b>Epclusa</b> (sofosbuvir/velpatasvir)	<ul style="list-style-type: none"> <li>▪ Epclusa and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated</li> </ul>
<b>Harvoni</b> (ledipasvir/sofosbuvir)	<ul style="list-style-type: none"> <li>▪ If used in combination with ribavirin, all contraindications to ribavirin also apply to Harvoni combination therapy.</li> </ul>
<b>Mavyret</b> (glecaprevir/pibrentasvir)	<ul style="list-style-type: none"> <li>▪ Patients with severe hepatic impairment (Child-Pugh C)</li> <li>▪ Coadministration with atazanavir or rifampin</li> </ul>
<b>Technivie</b> (ombitasvir/paritaprevir/ ritonavir)	<ul style="list-style-type: none"> <li>▪ If used in combination with ribavirin, the contraindications also apply to this combination regimen</li> <li>▪ Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)].</li> <li>▪ Co-administration with drugs that are: highly dependent on CYP3A for clearance; moderate and strong inducers of CYP3A.</li> <li>▪ Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Steven-Johnson syndrome).</li> <li>▪ The contraindications to ribavirin also apply to this combination regimen (Technivie + ribavirin).</li> </ul>
<b>Viekira Pak</b> (ombitasvir/paritaprevir/ritonavir + dasabuvir) and	<ul style="list-style-type: none"> <li>▪ Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)].</li> <li>▪ Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Steven-Johnson syndrome).</li> </ul>

<b>Agent(s)</b>	<b>Contraindication(s)</b>
<b>Viekira XR</b> (dasabuvir/ombitasvir paritaprevir/ritonavir)	<ul style="list-style-type: none"> <li>▪ 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.</li> <li>▪ If Viekira PAK or Viekira XR is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen.</li> </ul>
<b>Vosevi</b> (sofosbuvir/velpatasvir/voxilaprevir)	<ul style="list-style-type: none"> <li>▪ Coadministration with rifampin</li> </ul>
<b>Zepatier</b> (elbasvir/grazoprevir)	<ul style="list-style-type: none"> <li>▪ Patients with moderate or severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)].</li> <li>▪ Organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors, strong CYP3A inducers, and efavirenz.</li> <li>▪ If Zepatier is administered with ribavirin, the contraindications to ribavirin also apply.</li> </ul>

## **RATIONALE**<sup>5,6</sup>

### **Disease Background**

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**<sup>5</sup>

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.

New direct-acting antiviral agents (DAAs) capable of curing hepatitis C virus infection have been approved for use in the United States starting with the initial DAAs in 2011 and since that time many others have followed. DAAs offer the potential for highly effective, interferon-free (and in many cases, ribavirin-free) regimens for the majority of hepatitis C virus infected patients. Regimen selection varies by genotype and other patient factors, such as the presence of cirrhosis and treatment history. Patients who are co-infected with HCV and either hepatitis B or HIV should be treated as those mono-infected with HCV.

## **Efficacy**

### **Zepatier<sup>4</sup>**

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<sup>2</sup>) or CKD Stage 5 (eGFR <15 mL/min/1.73 m<sup>2</sup>), 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.

**Mavyret<sup>11</sup>**

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 EDNURANCE-1 trial demonstrated numerically similar efficacy in genotype 1 treatment naïve patients without cirrhosis treated for 8 weeks vs 12 weeks the SURVEYOR-2 trial also demonstrated very high SVR12 for genotypes 2, 4, 5, or 6 after 8 weeks of treatment. Therefore, the recommended length of therapy for treatment naïve patients without cirrhosis is 8 weeks.

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

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

The efficacy of Mavyret in treatment naïve and PRS treatment experienced adults with genotype 2, 4, 5, or 6 without cirrhosis was evaluated in the SURVEYOR-2 (part 2 and part 4), ENDURANCE-4, and SURVEYOR-1 (part 2) trials. SVR12 ranged from 93-100% depending on genotype.

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



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

The MAGRLLAN-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.

### **Harvoni<sup>1</sup>**

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 12 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.

### **Viekira Pak and Viekira XR<sup>3,8</sup>**

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

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

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

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

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

### **Technivie<sup>2</sup>**

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

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

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

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

### **Epclusa<sup>7</sup>**

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

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

ASTRAL-2 and ASRTAL-3 were randomized, open label trials evaluating efficacy in patients with HCV genotype 2 or 3 respectively. Those with HCV genotype 2 received either Epclusa for 12 weeks or sofosbuvir plus ribavirin for 12 weeks. The SVR12 rates for the two treatment arms were 99% and 94% respectively. Subjects with HCV genotype 3 were randomized to receive either Epclusa for 12 weeks or sofosbuvir plus ribavirin for 24 weeks. The SVR 12 rates were 95% and 80% respectively.

ASTRAL-4 was an open label trial that evaluated efficacy of Epclusa in patients with decompensated cirrhosis. Patients were randomized to receive one of three treatment regimens:

Epclusa for 12 weeks, Epclusa for 24 weeks, or Epclusa plus ribavirin for 12 weeks. SVR 12 rates were 83%, 86%, and 94% respectively.

ASTRAL-5 was an open-label trial that evaluated 12 weeks of Epclusa in patients with genotype 1, 2, 3, 4, 5, or 6 hepatitis C infection who were coinfecting 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.

### **Vosevi<sup>10</sup>**

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.

### **Safety**

#### **Risk of Hepatitis B infection reactivation with HCV Direct Acting Antivirals<sup>9</sup>**

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.

### **Epclusa<sup>7</sup>**

The most common adverse events reported in patients who received Epclusa were headache and fatigue. Those with decompensated cirrhosis who were treated with Epclusa and ribavirin reported fatigue, anemia, nausea, headache, insomnia, and diarrhea as the most common adverse events. Epclusa and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated.

### **Harvoni<sup>1</sup>**

The most common side effects associated with Harvoni are fatigue, headache, and asthenia. If used in combination with ribavirin, all contraindications to ribavirin also apply to Harvoni combination therapy.

**Mavyret<sup>11</sup>**

The most common adverse events associated with Mavyret are headache and fatigue. Mavyret is contraindicated in patients with severe hepatic impairment (Child-Pugh C) and in combination with atazanavir and rifampin.

**Technivie<sup>2</sup>**

The most common adverse events reported in the trials were asthenia, fatigue, nausea, insomnia, pruritis, and skin reaction. These adverse events were graded as mild in severity. Technivie is contraindicated in patients with severe hepatic impairment (Child-Pugh C) and if taken with ribavirin, the contraindications to ribavirin apply to the combination therapy.

**Viekira Pak and Viekira XR<sup>3,8</sup>**

The most common adverse events reported in the trials were fatigue, nausea, pruritic, skin reactions, insomnia, and asthenia. Viekira Pak and Viekira XR are contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C), in patients with known hypersensitivity to ritonavir [e.g. toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome] and if administered with ribavirin, the contraindications to ribavirin also apply to the combination therapy. In addition, Viekira Pak and Viekira XR should not be given with that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events. Viekira Pak and Viekira XR should not be given with drugs that are moderate or strong inducers of CYP3A and strong inducers of CYP2C8, or with drugs that are strong inhibitors of CYP2C8.

**Vosevi<sup>10</sup>**

The most common adverse events reported in patients who received sofosbuvir/velpatasvir/voxilaprevir were headache, fatigue, diarrhea, and nausea. Vosevi is contraindicated for co-administration with rifampin.

**Zepatier<sup>4</sup>**

The most common adverse events observed with Zepatier 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.

<b>REVISIONS</b>	
10-01-2014	Policy added to the bcbsks.com web site on October 2, 2014. Policy was effective on October 1, 2014.
10-24-2014	Policy published to the bcbsks.com web site on November 4, 2014. Policy was effective on October 24, 2014
	In Title: <ul style="list-style-type: none"> <li>▪ Added Harvoni to read "(Harvoni [ledipasvir/sofosbuvir]... "</li> </ul>
	In Description section: <ul style="list-style-type: none"> <li>▪ Added Harvoni to Target Drugs</li> <li>▪ Updated FDA Approved Indications and Dosage chart.</li> </ul>
	In Policy section: <ul style="list-style-type: none"> <li>▪ In Item A added "Harvoni" to read " "Harvoni (ledipasvir/sofosbuvir and paritaprevir/ritonavir/ombitasvir + dasabuvir will be approved when the following criteria are met:"</li> <li>▪ In Item A Length of Approval revised "6" to "24" and added "as determined in Table 1" to read, "Up to 214 weeks as determined in Table 1"</li> </ul>

<b>REVISIONS</b>	
	<ul style="list-style-type: none"> <li>▪ In Item A added "Table 1 Harvoi Treatment Duration Recommendations"</li> <li>▪ In Item B Length of approval added "for Sovaldi containing regimens" to read, "As determined in Table 3 below for Sovaldi containing regimens based on regimen and genotype"</li> </ul>
	Coding section removed as codes are not used for pharmacy benefit.
	References updated
02-24-2015	<ul style="list-style-type: none"> <li>▪ Title changed to "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s) (2015) (Harvoni® [ledipasvir / sofosbuvir]; and Viekira Pak [ombitasvir / paritaprevir / ritonavir + dasabuvir]" from " Hepatitis C Second Generation Antivirals – Through Preferred Pegylated Interferon (2014) (Harvoni [ledipasvir/sofosbuvir], paritaprevir/ritonavir/ombitasvir + dasabuvir, and Sovaldi [sofosbuvir])"</li> <li>▪ Related policy titles added under title.</li> </ul>
	Description section updated
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item A added "Initial Evaluation" and "or Viekira Pak" and removed "(ledipasvir/sofosbuvir and paritaprevir/ritonavir/ombitasvir + dasabuvir)" to read "Initial Evaluation - Harvoni or Viekira Pak will be approved when the following criteria are met:"</li> <li>▪ In Item A 1 added "markers – pretreatment HCV RNA level must be provided" and removed "(irrespective of subtype)" to read "The patient has a diagnosis of chronic hepatitis C, genotype 1 confirmed by serological markers – pretreatment HCV RNA level must be provided AND"</li> </ul> <p>Removed old Item 2 "The patient has not been previously treated for chronic hepatitis C with another regimen containing any of the agents referenced above (individually or as part of any combination therapy)"</p> <ul style="list-style-type: none"> <li>▪ In new Item 2 added "If able, the prescriber will provide an SVR post treatment week 12."</li> <li>▪ In Item 4 added a Contraindications chart.</li> <li>▪ Added Item 8</li> </ul> <p>"If the request is for Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir) ALL of the following:</p> <ol style="list-style-type: none"> <li>a. The patient has not been previously treated with a regimen containing sofosbuvir, simeprevir, telaprevir, or boceprevir</li> <li>b. The patient's subtype has been identified and provided</li> <li>c. The patient does not have decompensated liver disease OR</li> </ol> <ul style="list-style-type: none"> <li>▪ Added Item 9</li> </ul> <p>If the request is for Harvoni, the following:</p> <ol style="list-style-type: none"> <li>a. The patient has not been previously treated with Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir) AND</li> <li>b. ONE of: <ol style="list-style-type: none"> <li>i. The patient has NOT failed a previous sofosbuvir containing regimen OR</li> <li>ii. BOTH of the following: <ol style="list-style-type: none"> <li>1. The patient has failed a previous sofosbuvir containing regimen AND</li> <li>2. The patient has advanced fibrosis (Metavir F3 or F4)</li> </ol> </li> </ol> </li> </ol> <ul style="list-style-type: none"> <li>▪ In Item 10 move "25 mg ombitasvir" to another location within the statement.</li> <li>▪ Updated Table 1 to indicated "Treatment naïve without cirrhosis and initial viral load &lt; 6 M IU/mL" is "8 weeks"</li> <li>▪ Added Table 2 reflecting "Viekira Treatment Duration Recommendations based on labeling" and "Length of Approval"</li> <li>▪ Removed all criteria and Length of Approval for "Initial Evaluation Sovaldi (sofosbuvir ± Pegylated Interferon ± Olysio"</li> </ul> <ol style="list-style-type: none"> <li>1. The patient is naïve to therapy with Sovaldi AND</li> <li>2. The agent is being prescribed by a specialist or in consultation with a specialist (i.e. Gastroenterologist, Hepatologist, Infectious Disease) AND</li> <li>3. The patient has a diagnosis of chronic hepatitis C infection confirmed by serological markers AND</li> <li>4. Sofosbuvir will be used in a combination antiviral treatment regimen supported by FDA approved labeling or the AASLD guidelines (listed in Rationale below) <ol style="list-style-type: none"> <li>a. If genotype 1, treatment naïve requesting the combination of simeprevir and sofosbuvir, the patient has BOTH of the following: <ol style="list-style-type: none"> <li>i. a METAVIR score of 3 or 4 AND</li> <li>ii. Ineligible to receive peginterferon AND</li> </ol> </li> </ol> </li> </ol>

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	<p>5. The patient does NOT have any FDA labeled contraindications to sofosbuvir or the other agents used in the combination therapy AND</p> <p>6. The patient will NOT be receiving Incivek (telaprevir) or Victrelis (boceprevir) concomitantly with sofosbuvir AND</p> <p>7. The patient is not coinfecting with chronic hepatitis B AND</p> <p>8. If the patient has hepatocellular carcinoma the following are met:</p> <ol style="list-style-type: none"> <li>The patient has either a single tumor 5 cm or less in diameter OR The patient has up to 3 tumors with each being 3 cm or less in diameter AND</li> <li>The patient has NO extrahepatic manifestations of cancer or evidence of vascular invasion of tumor AND</li> </ol> <p>9. The dosing of sofosbuvir is within the FDA labeled dosage ( 400 mg daily) AND</p> <p>10. If the treatment regimen includes simeprevir, the dosing of simeprevir is within the FDA labeled dosage (150 mg daily)"</p> <p>"Length of approval: As determined below in Table 3 for Sovaldi containing regimens based on regimen and genotype"</p> <ul style="list-style-type: none"> <li>▪ Removed all criteria and Length of Approval for "Nonpreferred Agent(s) peginterferon (TRIPLE THERAPY)"</li> </ul> <p>"Nonpreferred Agent(s) peginterferon (TRIPLE THERAPY) will be approved when the criteria for the preferred peginterferon listed above are met AND ONE of the following additional criteria are met:</p> <ol style="list-style-type: none"> <li>The patient is currently being treated with the non-preferred agent OR</li> <li>The patient has a history of a trial of the preferred peginterferon OR</li> <li>The patient has an FDA labeled contraindication, documented intolerance, or hypersensitivity to the preferred agent(s) peginterferon OR</li> <li>The prescriber has submitted documentation in support of the use of the non-preferred agent(s) peginterferon, for the intended diagnosis"</li> </ol> <p>"Length of approval: Up to 48 weeks based on regimen"</p> <p>Removed related tables of "AASLD Supported Sovaldi® Containing Antiviral Regimens", "IFN ineligible definitions", and "Approval Durations"</p>
	Rationale section updated to include updates to 2014 AASLD guidelines.
	Reference updated
09-01-2015	Policy added to the bcbsks.com web site on 08-25-2015 and effective 09-01-2015.
	Description section updated
	In Policy section:
	<ul style="list-style-type: none"> <li>▪ In Item A added Viekira Pak genetic drug names "(ombitasvir / paritaprevir / ritonavir + dasabuvir)"</li> <li>▪ In Item A 1 removed "-pretreatment HCV RNA level must be provided" to read, "The patient has a diagnosis of chronic hepatitis C, genotype 1 confirmed by serological markers" and made this a stand-alone Item A 2 "The prescriber has provided a baseline HCV RNA level"</li> <li>▪ In Item A 8 d added "esophageal varices" to read "(e.g. portal hypertension, esophageal varices)"</li> <li>▪ In Item 9 added "The agent will be used in a combination antiviral treatment regimen supported by FDA approved labeling (see Table 2 below) AND"</li> <li>▪ In Item 10 added "ALL of" to read "If the request is for Harvoni, ALL of the following:"</li> <li>▪ In Item 10 a added "or Harvoni (ledipasvir / sofosbuvir)" to read "The patient has not been previously treated with Viekira (ombitasvir / paritaprevir / ritonavir + dasabuvir) or Harvoni (ledipasvir / sofosbuvir)"</li> <li>▪ In Item 10 b ii a added "not including Harvoni (ledipasvir / sofosbuvir" to read, "The patient has failed a previous sofosbuvir containing regimen, not including Harvoni (ledipasvir/sofosbuvir)"</li> <li>▪ Updated the Harvoni Treatment Duration Recommendations table.</li> <li>▪ Added:</li> </ul> <p>"Non-Preferred Agent(s) – will be approved when the ONE of the following additional criteria are met:</p> <ol style="list-style-type: none"> <li>The patient is currently being treated with the non-preferred agent OR</li> <li>The patient has an FDA labeled contraindication, documented intolerance, or hypersensitivity to the preferred agent(s) OR</li> <li>The prescriber has submitted documentation in support of the use of the non-preferred agent(s), for the intended diagnosis."</li> </ol>
	Rationale section updated
	References updated
01-01-2016	Policy published 12-30-2015. Policy effective 01-01-2016.

<b>REVISIONS</b>	
	<p>Revised Policy Title from:  "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s) (2015)  (Harvoni® [ledipasvir / sofosbuvir] and Viekira Pak [ombitasvir/ paritaprevir/ritonavir + dasabuvir]  to:  "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s) (2015)  (Harvoni®, Viekira™, and Technivie™)"</p>
	<p>With the addition of new information on Technivie created two Description / Policy sections titled:  "I. 2015 Hepatitis C Second Generation Antivirals PA - Through Preferred Oral agent(s)  (Harvoni® [ledipasvir/sofosbuvir] and Viekira Pak™ [ombitasvir/paritaprevir/ritonavir + dasabuvir])"  And  "II.2015 Hepatitis C Second Generation Antivirals PA  (Technivie™ [ombitasvir/ paritaprevir/ritonavir])"  Rationale and References sections remain combined</p>
	<p>In I. 2015 Hepatitis C Second Generation Antivirals PA Description section:</p> <ul style="list-style-type: none"> <li>▪ Updated Description</li> <li>▪ In Target Drugs Chart moved Viekira Pak from being a Preferred Agent to being a Non-Preferred Agent</li> </ul>
	<ul style="list-style-type: none"> <li>▪ In I. 2015 Hepatitis C Second Generation Antivirals PA Policy section:</li> <li>▪ In Item 1 removed "genotype 1" to read "The patient has a diagnosis of chronic hepatitis C, confirmed by serological markers"</li> <li>▪ In Item 9 added "a. The patient has chronic hepatitis C genotype 1"</li> <li>▪ In Item 9 c add "for chronic hepatitis C" and "daclatasvir, dasabuvir, ombitasvir, paritaprevir, ritonavir," to read, "The patient has not been previously treated for chronic hepatitis C with a regimen containing daclatasvir, dasabuvir, ombitasvir, paritaprevir, ritonavir, sofosbuvir, simeprevir, telaprevir, or boceprevir"</li> <li>▪ In Item 10 removed "ALL" and added "ONE" to read, "If the request is for Harvoni, ONE of the following:"</li> <li>▪ In Item 10 a added "i. The patient has chronic hepatitis C genotype 1"</li> <li>▪ In Item 10 a ii added "Daklinza (daclatasvir)" and "or Technivie (ombitasvir/paritaprevir/ ritonavir)" to read, "The patient has not been previously treated with Daklinza (daclatasvir), Viekira (ombitasvir / paritaprevir / ritonavir + dasabuvir), Harvoni (ledipasvir / sofosbuvir), or Technivie (ombitasvir/paritaprevir/ritonavir)"</li> <li>▪ In Item 10 added  "BOTH of the following:  The patient has chronic hepatitis C genotype 4, 5, or 6 AND  The patient has not been previously treated with Daklinza (daclatasvir), Harvoni (ledipasvir/sofosbuvir), Sovaldi (sofosbuvir), Technivie (ombitasvir/paritaprevir/ritonavir), Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir), or a protease inhibitor (e.g. Incivek, Victrelis, Simeprevir)"</li> <li>▪ In Table 1 Harvoni Treatment Duration Recommendations added Patient Population and Treatment Duration for Genotype 4, 5, and 6</li> </ul>
	<p>Added II.2015 Hepatitis C Second Generation Antivirals PA Description section to include the Non-Preferred Agent of Technivie (ombitasvir/paritaprevir/ritonavir) (There are no preferred agents) and FDA Approved Indications an Dosage Charts</p>
	<p>In II.2015 Hepatitis C Second Generation Antivirals PA Policy section:</p> <ul style="list-style-type: none"> <li>▪ Added new policy information of  "Initial Evaluation – Technivie (ombitasvir/paritaprevir/ritonavir) will be approved when ALL of the following criteria are met:</li> </ul> <ol style="list-style-type: none"> <li>1. The patient has a diagnosis of chronic hepatitis C, genotype 4 confirmed by serological markers AND</li> <li>2. The patient does not have any of the following: <ol style="list-style-type: none"> <li>a. Cirrhosis OR</li> <li>b. Decompensated liver disease OR</li> <li>c. Moderate or severe hepatic impairment (Child-Pugh B or C) AND</li> </ol> </li> <li>3. The requested agent is being prescribed by a specialist (i.e. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND</li> </ol>

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	<p>4. The requested agent will be used in a combination antiviral treatment regimen supported by FDA approved labeling (see Table 1 below) AND</p> <p>5. The patient has not been previously treated with the requested agent or with a regimen containing a direct acting antiviral (DAA) indicated for chronic hepatitis C (e.g. Daklinza, Harvoni, Incivek, Olysio, Sovaldi, Victrelis, or Viekira) AND</p> <p>6. The patient will not use the requested agent in combination, with a regimen containing a direct acting antiviral (DAA) indicated for chronic hepatitis C (e.g. Daklinza, Harvoni, Incivek, Olysio, Sovaldi, Victrelis, or Viekira) AND</p> <p>7. The patient does not have Hepatocellular Carcinoma (HCC) AND</p> <p>8. The patient is not co-infected with Hepatitis B virus (HBV) AND</p> <p>9. ONE of the following:</p> <ol style="list-style-type: none"> <li>The patient has a METAVIR score of 2 or 3 OR</li> <li>The patient has a Ishak score of 3 to 5 OR</li> <li>The patient has a Fibroscan score of 7.65 kPa to 13.00 kPa OR</li> <li>The patient is post-liver transplant OR</li> <li>The patient is co-infected with HIV-1 AND</li> </ol> <p>10. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent AND</p> <p>11. The dose is within the FDA labeled dose (25 mg ombitasvir/150 mg of paritaprevir/100 mg ritonavir)</p> <p>Length of Approval: Up to 12 weeks as determined by Table 1"</p> <ul style="list-style-type: none"> <li>▪ Added Technivie Treatment Duration Recommendations based on FDA labeling and Contraindications charts.</li> <li>▪ Added the Non-preferred policy language of: "Non-Preferred Agent(s) – will be approved when the ONE of the following additional criteria are met:</li> </ul> <ol style="list-style-type: none"> <li>The patient is currently being treated with the non-preferred agent OR</li> <li>The patient has an FDA labeled contraindication, documented intolerance, or hypersensitivity to the preferred agent(s) OR</li> <li>The prescriber has submitted documentation in support of the use of the non-preferred agent(s), for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist</li> </ol> <p>Updated Rationale section</p> <p>Updated References</p>
03-21-2016	<p>Removed from title the wording "(2015)" and "(Harvoni®, Viekira™, Technivie™) to read "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s)"</p> <p><u>In Section I Hepatitis C Second Generation Antivirals PA - Through Preferred Oral agent(s)</u></p> <p>Description section updated</p> <p>Updated Target Drugs–Non-Preferred Agent adding Zepatier</p> <p>Updated FDA Approved Indications and Dosage chart to include adding Zepatier (elbasvir/grazoprevir)</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Initial Evaluation Header added "Zepatier" and removed "(ombitasvir / paritaprevir / ritonavir + dasabuvir)"</li> <li>▪ In Item 3 revised "i.e." to "e.g." and removed "If able, the prescriber will provide an SVR post treatment week 12" to read "The agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist."</li> <li>▪ In Item 5 added Zepatier to the contraindications chart.</li> <li>▪ In Item 9 removed "The agent will be used in a combination antiviral treatment regimen supported by FDA approved labeling (see Table 2 below) AND"</li> <li>▪ In Item 9 b added "elbasvir, grazoprevir"</li> <li>▪ In Item 10 added "(ledipasvir/sofosbuvir)" to read "Harvoni (ledipasvir/sofosbuvir)"</li> <li>▪ In Item 10 a ii added "or Zepatier (elbasvir/grazoprevir)" to read "The patient has not been previously treated with Daklinza (daclatasvir), Viekira (ombitasvir / paritaprevir / ritonavir + dasabuvir) Harvoni (ledipasvir / sofosbuvir), Technivie (ombitasvir/paritaprevir/ritonavir), or Zepatier (elbasvir/grazoprevir)"</li> <li>▪ In Item 10 a iii 2) b added "Ishak score ≥5, Fibroscan score ≥ 12.5 kPa)" to read "The patient has advanced fibrosis (Metavir F3 or F4, Ishak score ≥5, Fibroscan score ≥ 12.5 kPa)"</li> <li>▪ In Item 10 b ii added a protease inhibitor "Zepatier (elbasvir/grazoprevir)" and removed "(e.g. Incivek, Victrelis, Simeprevir)" to read "The patient has not been previously treated with Daklinza</li> </ul>



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	<p>(daclatasvir), Harvoni (ledipasvir/sofosbuvir), Sovaldi (sofosbuvir), Technivie (ombitasvir/paritaprevir/ritonavir), Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir), or Zepatier (elbasvir/grazoprevir)"</p> <ul style="list-style-type: none"> <li>▪ Added</li> </ul> <p>"11. If the request is for Zepatier (elbasvir/grazoprevir), ALL of the following:</p> <ol style="list-style-type: none"> <li>a. The patient has chronic hepatitis C genotype 1 or 4 AND</li> <li>b. If genotype 1, the patient's subtype has been provided AND</li> <li>c. If genotype 1a, the prescriber has tested the patient for NS5A polymorphisms AND</li> <li>d. The patient has not been previously treated for chronic hepatitis C with a regimen containing Daklinza, Harvoni, Sovaldi, Technivie, Viekira or Zepatier AND</li> </ol> <p>12. The agent will be used in a treatment regimen AND length of therapy supported in FDA approved labeling for the patient's genotype (see Table 1, 2, and 3 below) AND"</p> <p>In Item 13 added "or 50 mg elbasvir/100 mg grazoprevir)" to read "The dose is within the FDA labeled dose (90 mg of ledipasvir / 400 mg of sofosbuvir, 25 mg ombitasvir / 150 mg of paritaprevir / 100 mg ritonavir plus 250 mg twice daily of dasabuvir, or 50 mg elbasvir/100 mg grazoprevir)"</p> <ul style="list-style-type: none"> <li>▪ In Length of Approval added "and 3 below" to read "Up to 24 weeks as determined in Tables 1, 2, and 3 below."</li> <li>▪ Updated Table 1 Harvoni Treatment Duration Recommendations based on FDA Labeling and Table 2 Viekira Treatment Duration Recommendations based on FDA labeling</li> <li>▪ Added Table 3 Zepatier Treatment Duration Recommendations based on FDA labeling</li> <li>▪ In Non-Preferred Agents added "3. If requesting Zepatier, the patient has severe renal impairment (i.e. stage 4 or 5 Chronic Kidney disease as indicated by eGFR of &lt;30 mL/min/1.73 m2) or end stage renal disease requiring hemodialysis OR"</li> </ul> <p><u>In Section II Hepatitis C Second Generation Antivirals PA</u></p> <p>Updated FDA Approved Indications and Dosage chart</p> <ul style="list-style-type: none"> <li>▪ In Policy section:</li> <li>▪ In Item 3 revised "i.e." to "e.g." to read "The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist."</li> <li>▪ In Item 5 added "or Zepatier" to read "The patient has not been previously treated with the requested agent or with a regimen containing a direct acting antiviral (DAA) indicated for chronic hepatitis C (e.g. Daklinza, Harvoni, Incivek, Olysio, Sovaldi, Victrelis, Viekira, or Zepatier)"</li> <li>▪ In Item 6 added "or Zepatier" to read "The patient will not use the requested agent in combination, with a regimen containing a direct acting antiviral (DAA) indicated for chronic hepatitis C (e.g. Daklinza, Harvoni, Incivek, Olysio, Sovaldi, Victrelis, Viekira, or Zepatier)"</li> </ul> <p>Updated Rationale section</p> <p>Updated References</p>
06-01-2016	<p>Published 05-25-2016. Effective 06-01-2016.</p> <p><u>I. Initial Evaluation - Harvoni, Viekira Pak, and Zepatier Policy section:</u></p> <ul style="list-style-type: none"> <li>▪ In Item 2 added "If requesting Harvoni" to read "If requesting Harvoni, the prescriber has provided a baseline HCV RNA level"</li> <li>▪ Removed the following criteria: "ONE of the following:</li> <ol style="list-style-type: none"> <li>a. The patient has a METAVIR score of <math>\geq 2</math> OR</li> <li>b. The patient has a Ishak score <math>\geq 3</math> OR</li> <li>c. The patient has a Fibroscan score of <math>\geq 7.65</math> kPa OR</li> <li>d. The patient has radiological imaging consistent with fibrosis and/or cirrhosis (e.g. portal hypertension, esophageal varices) OR</li> <li>e. The patient has type 2 or 3 mixed cryoglobulinemia with end-organ manifestations (e.g. vasculitis) OR</li> <li>f. The patient has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis OR</li> <li>g. The patient is currently awaiting liver transplant OR</li> <li>h. The patient is post-liver transplant OR</li> <li>i. The patient is co-infected with HIV-1"</li> </ol> </ul> <p><u>II. Technivie Description section updated</u></p> <p><u>II. Technivie Policy section</u></p> <ul style="list-style-type: none"> <li>▪ Removed the following criteria: "ONE of the following:</li> </ul>

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	<p>a. The patient has a METAVIR score of <math>\geq 2</math> OR</p> <p>b. The patient has a Ishak score <math>\geq 3</math> OR</p> <p>c. The patient has a Fibroscan score of <math>\geq 7.65</math> kPa OR</p> <p>d. The patient has radiological imaging consistent with fibrosis and/or cirrhosis (e.g. portal hypertension, esophageal varices) OR</p> <p>e. The patient has type 2 or 3 mixed cryoglobulinemia with end-organ manifestations (e.g. vasculitis) OR</p> <p>f. The patient has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis OR</p> <p>g. The patient is currently awaiting liver transplant OR</p> <p>h. The patient is post-liver transplant OR</p> <p>i. The patient is co-infected with HIV-1"</p> <p>Added <u>III. Hepatitis C Second Generation New To Market Antivirals</u> section with the following policy language:  "Initial Evaluation – 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. The requested agent is FDA approved for treatment of the patient’s genotype AND  3. The patient does not have any FDA labeled contraindications to therapy 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 dose is within the FDA labeled dose (see Table 1) AND  6. The agent will be used in a treatment regimen AND duration of therapy supported in FDA approved labeling for the patient’s diagnosis and genotype (see Table 1 below)  Length of Approval: Up the FDA approved duration of treatment as determined in table 1 below"</p> <p>Rationale section updated to include updating the AASLD recommendations removing priority treatment criteria.</p>
06-01-2016	<p>Published 06-08-2016. Retro-effective to 06-01-2016.</p> <ul style="list-style-type: none"> <li>▪ Corrected Revision section (06-01-2016 above) to include the addition of III. Hepatitis C Second Generation New To Market Antivirals</li> </ul>
07-25-2016	<p>Published 08-04-2016. Retro-effective to 07-25-2016.</p> <p>In III. Hepatitis C Second Generation New To Market Antivirals Description section</p> <ul style="list-style-type: none"> <li>▪ Added Eplusa (sofosbuvir/velpatasvir) as a Non-preferred drug</li> <li>▪ Updated FDA Approved Indications and Dosage chart for Eplusa</li> </ul> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ Updated Treatment Duration Recommendations based on FDA labeling and Contraindications charts for Eplusa</li> </ul> <p>References updated</p>
09-01-2016	<p>Title changed to "Hepatitis C Second Generation – Through Preferred Agent(s)" from "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s)"</p> <p>Description section updated</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item A removed "Initial Evaluation" and Viekira Pak, or Zepatier" to read "Harvoni will be approved when ALL of the following criteria are met:"</li> <li>▪ In Item A 1 removed "confirmed by serological markers" and added "genotype 1, 4, 5, or 6" to read "The patient has a diagnosis of chronic hepatitis C genotype 1, 4, 5, or 6"</li> <li>▪ In Item A 2 removed "If requesting Harvoni" and added "the patient's" and "if the patient has genotype 1" to read "The prescriber has provided the patient's a baseline HCV RNA level if the patient has genotype 1"</li> <li>▪ Removed "These agents will not be used in combination with other protease inhibitors used to treat chronic hepatitis C (i.e. boceprevir, simeprevir, or telaprevir)"</li> <li>▪ Added Item A 5 "ONE of the following: <ul style="list-style-type: none"> <li>a. The patient is treatment naive OR</li> <li>b. The patient was previously treated (i.e. treatment experienced) with ONLY ONE of the following regimens: <ul style="list-style-type: none"> <li>i. The previous treatment is peg-interferon and ribavirin with or without an HCV protease inhibitor OR</li> </ul> </li> </ul> </li> </ul>

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- 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"
    - Removed
- "The patient does not have hepatocellular carcinoma (see Sovaldi criteria for approval) AND  
The patient is not co-infected with chronic hepatitis B AND  
If the request is for Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir) ALL of the following:
- a. The patient has chronic hepatitis C genotype 1 AND
  - b. The patient has not been previously treated for chronic hepatitis C with a regimen containing daclatasvir, dasabuvir, elbasvir, grazoprevir, ombitasvir, paritaprevir, ritonavir, sofosbuvir, simeprevir, telaprevir, or boceprevir AND
  - c. The patient's subtype has been identified and provided AND
  - d. The patient does not have decompensated liver disease AND
- If the request is for Harvoni (ledipasvir/sofosbuvir), ONE of the following:
- a. ALL of the following:
    - i. The patient has chronic hepatitis C genotype 1 AND
    - ii. The patient has not been previously treated with Daklinza (daclatasvir), Viekira (ombitasvir / paritaprevir / ritonavir + dasabuvir), Harvoni (ledipasvir / sofosbuvir), Technivie (ombitasvir/paritaprevir/ritonavir), or Zepatier (elbasvir/grazoprevir) AND
    - iii. ONE of the following:
      - 1) The patient has NOT failed a previous sofosbuvir containing regimen OR
      - 2) BOTH of the following:
        - a) The patient has failed a previous sofosbuvir containing regimen, not including Harvoni (ledipasvir/sofosbuvir) AND
        - b) The patient has advanced fibrosis (Metavir F3 or F4, Ishak score  $\geq 5$ , Fibroscan score  $\geq 12.5$  kPa) OR
      - b. BOTH of the following:
        - i. The patient has chronic hepatitis C genotype 4, 5, or 6 AND
        - ii. The patient has not been previously treated with Daklinza (daclatasvir), Harvoni (ledipasvir/sofosbuvir), Sovaldi (sofosbuvir), Technivie (ombitasvir/paritaprevir/ritonavir), Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir), or Zepatier (elbasvir/grazoprevir) AND
- If the request is for Zepatier (elbasvir/grazoprevir), ALL of the following:
- a. The patient has chronic hepatitis C genotype 1 or 4 AND
  - b. If genotype 1, the patient's subtype has been provided AND
  - c. If genotype 1a, the prescriber has tested the patient for NS5A polymorphisms AND
  - d. The patient has not been previously treated for chronic hepatitis C with a regimen containing Daklinza, Harvoni, Sovaldi, Technivie, Viekira or Zepatier"
    - Added Item 6 "The dose is within the FDA labeled dose"
    - In Item 7 removed "supported in FDA approved labeling" and added "recommended", "(FDA labeling), "AASLD/IDSA guidelines" to read "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) and Table 2 (AASLD/IDSA guidelines)"
    - Removed "The dose is within the FDA labeled dose (90 mg of ledipasvir / 400 mg of sofosbuvir, 25 mg ombitasvir / 150 mg of paritaprevir / 100 mg ritonavir plus 250 mg twice daily of dasabuvir, or 50 mg elbasvir/100 mg grazoprevir)"
    - In Length of Approval removed "24 weeks" and added "the duration of treatment" to read "Up to the duration of treatment as determined in Tables 1 and 2"
    - Added "Table 2: Harvoni Treatment Recommendations based on AASLD/IDSA Guidelines"
    - In B 1 removed "confirmed by serological markers" and added "compensated" to read "The patient has a diagnosis of compensated chronic hepatitis C, genotype 4"
    - Removed "The patient does not have any of the following:
      - a. Cirrhosis OR
      - b. Decompensated liver disease OR
      - c. Moderate or severe hepatic impairment (Child-Pugh B or C)"
        - Removed "The requested agent will be used in a combination antiviral treatment regimen supported by FDA approved labeling (see Table 1 below) AND

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The patient has not been previously treated with the requested agent or with a regimen containing a direct acting antiviral (DAA) indicated for chronic hepatitis C (e.g. Daklinza, Harvoni, Incivek, Olysio, Sovaldi, Victrelis, Viekira, or Zepatier) AND

The patient will not use the requested agent in combination, with a regimen containing a direct acting antiviral (DAA) indicated for chronic hepatitis C (e.g. Daklinza, Harvoni, Incivek, Olysio, Sovaldi, Victrelis, Viekira, or Zepatier) AND

The patient does not have Hepatocellular Carcinoma (HCC) AND

The patient is not co-infected with Hepatitis B virus (HBV)"

- Added "4. 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
- 5. The dose is within the FDA labeled dose AND
- 6. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype as noted in Table 3 (FDA labeling)"
  - Removed "The dose is within the FDA labeled dose (25 mg ombitasvir/150 mg of paritaprevir/100 mg ritonavir)"
  - In Item C added "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 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 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 4 (FDA labeling)

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

- Added Item D "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 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 5 (FDA labeling)

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

- Removed Non-Preferred Agents criteria of "Non-Preferred Agent(s) – will be approved when the 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, documented intolerance, 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 m<sup>2</sup>) or end stage renal disease requiring hemodialysis OR
  4. The prescriber has submitted documentation in support of the use of the non-preferred agent(s), for the intended diagnosis."

<b>REVISIONS</b>														
	<ul style="list-style-type: none"> <li>▪ In Item E 6 removed "supported in FDA approved labeling for the" and added "length" and "recommended for the" and "FDA labeling" to read "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 6 FDA labeling"</li> <li>▪ In Item F added "drug specific criteria above and "Non-Preferred Agent(s) will be approved when the drug specific criteria above and ONE of the following additional criteria are met:"</li> <li>▪ In Item F 2 removed "documented intolerance" to read "The patient has an FDA labeled contraindication or hypersensitivity to the preferred agent(s)"</li> <li>▪ Added Item F 3 "If requesting Zepatier, the patient has severe renal impairment (i.e. stage 4 or 5 Chronic Kidney disease as indicated by eGFR of &lt;30 mL/min/1.73 m2) or end stage renal disease requiring hemodialysis"</li> <li>▪ In Item F 4 removed "for the intended diagnosis which has been reviewed and approved" and added "over the preferred agent(s)" to read "The prescriber has submitted documentation in support of the use of the non-preferred agent over the preferred agent(s)"</li> <li>▪ Contraindications chart updated</li> </ul>													
	Rationale section updated													
	References updated													
09-01-2016	Published 10-12-2016. Retro-effective to 09-01-2016.													
	In Description section: <ul style="list-style-type: none"> <li>▪ Updated Target Drugs chart to add Viekira XR (ombitasvir/paritaprevir/ritonavir/dasabuvir) as a non-preferred agent.</li> <li>▪ Updated FDA Approved Indications and Dosage adding Viekira XR (ombitasvir/paritaprevir/ritonavir/dasabuvir)</li> </ul>													
	In Policy section: <ul style="list-style-type: none"> <li>▪ Updated Table 4 adding "Viekira XR" to read "Viekira PAK and Viekira XR Treatment Recommendations based on FDA labeling" and updated drug combination treatments</li> <li>▪ Updated Table 6: Treatment Recommendations based on FDA labeling following New to market chronic Hepatitis C agents section adding Epclusa (sofosbuvir/velpatasvir)</li> <li>▪ Updated the Contraindications chart removing Epclusa (sofosbuvir/velpatasvir) and adding Viekira XR (paritaprevir/ritonavir/ombitasvir/dasabuvir)</li> </ul>													
	Rationale section updated													
	References updated													
11-01-2016	Policy published 11-18-2016. Policy retro-effective to 11-01-2016.													
	<ul style="list-style-type: none"> <li>▪ Description section Target Drugs chart updated moving Epclusa from a Non-Preferred Agent to a Preferred Agent.</li> <li>▪ FDA Approved Indications and Dosage chart updated</li> </ul>													
	In Policy section: <ul style="list-style-type: none"> <li>▪ Added the following Epclusa criteria and Length of approval chart:</li> </ul> <p>"A. Epclusa will be approved when ALL of the following criteria are met:</p> <ol style="list-style-type: none"> <li>1. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 AND</li> <li>2. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND</li> <li>3. The patient does not have any FDA labeled contraindications to the requested agent AND</li> <li>4. ONE of the following: <ol style="list-style-type: none"> <li>a. The patient is treatment naïve OR</li> <li>b. The patient was previously treated (i.e. treatment experienced) with ONLY peg-interferon and ribavirin with or without an HCV protease inhibitor AND</li> </ol> </li> <li>5. The dose is within the FDA labeled dose AND</li> <li>6. 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)</li> </ol> <p>Length of approval: Up to the duration of treatment as determined in Table 1</p> <p>Table 1: Epclusa Treatment Recommendations based on FDA labeling</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 20%;">Genotype</th> <th style="width: 45%;">Patient population</th> <th style="width: 15%;">Treatment</th> <th style="width: 20%;">Duration</th> </tr> </thead> <tbody> <tr> <td rowspan="2" style="text-align: center;">1, 2, 3, 4, 5, or 6</td> <td>Patients without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td> <td style="text-align: center;">Epclusa</td> <td style="text-align: center;">12 weeks</td> </tr> <tr> <td>Patients with decompensated cirrhosis (Child-Pugh B and C)</td> <td style="text-align: center;">Epclusa + ribavirin</td> <td style="text-align: center;">12 weeks"</td> </tr> </tbody> </table>	Genotype	Patient population	Treatment	Duration	1, 2, 3, 4, 5, or 6	Patients without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks	Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + ribavirin	12 weeks"		
Genotype	Patient population	Treatment	Duration											
1, 2, 3, 4, 5, or 6	Patients without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks											
	Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + ribavirin	12 weeks"											

<b>REVISIONS</b>	
	<ul style="list-style-type: none"> <li>▪ In Items B, C, D, E, and F updated Table numbers.</li> <li>▪ Updated Contraindications chart</li> </ul>
	Rationale section updated
	References updated
05-15-2017	<p>In Title section added "Antivirals" to read Hepatitis C Second Generation Antivirals – Through Preferred Agent</p> <p>In Description section:</p> <ul style="list-style-type: none"> <li>▪ Updated Preferred Agents chart as follows: <ul style="list-style-type: none"> <li>✓ To Eplclusa added "(preferred for genotype 1, 4, 5, and 6)"</li> <li>✓ To Harvoni added "(preferred for genotype 2 and 3)"</li> </ul> </li> <li>▪ Updated FDA Approved Indications and Dosage chart for Technivie and Harvoni indications.</li> </ul> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Items A 2, B 3, C 2, D 3, and E 3 added "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".</li> <li>▪ In Item B 8 "and 3" to Table listing and revised Table 3 to Table 4.</li> <li>▪ In Item B Length of Approval added "and 4" to Table listing.</li> <li>▪ Updated Table 2</li> <li>▪ Added new Table 3 and re-numbered Tables accordingly</li> <li>▪ In Item C revised "Table 4" to "Table 5"</li> <li>▪ In Item D added "PAK and Viekira XR" to read "Viekira PAK and Viekira XR will be approved when ALL of the following criteria are met:" and revised "Table 5" to "Table 6"</li> <li>▪ In Item E revised "Table 6" to "Table 7"</li> <li>▪ In Item F added "BOTH of the following: <ol style="list-style-type: none"> <li>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</li> <li>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 revised "Table 7" to "Table 8"</li> </ol> </li> <li>▪ Updated Table 5 Technivie Treatment Recommendations based on FDA labeling and Table 6 Viekira PAK and Viekira XR Treatment Recommendations based on FDA labeling.</li> </ul>
	Rationale section updated
	References updated
05-15-2017	<p>Published 07-17-2017. Retro-effective to 05-15-2017.</p> <p>Corrected wording in the Target Drugs chart to reflect Eplclusa (sofosbuvir/velpatasvir) is "(preferred for genotype 2 and 3)" rather than "(preferred for genotype 1, 4, 5, and 6)" and Harvoni (ledipasvir/sofosbuvir) is "(preferred for genotype 1, 4, 5, and 6)" rather than "(preferred for genotype 2 and 3)".</p>
08-14-2017	<p>Policy published 09-01-2017. Policy retro-effective to 08-14-2017.</p> <p>In Description section:</p> <ul style="list-style-type: none"> <li>▪ Added New to Market Hepatitis C Target Agent of Vosevi (glecaprevir/pibrentasvir)</li> <li>▪ Added Vosevi to the FDA Approved Indications and Dosage chart</li> </ul> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Table 1: Eplclusa Treatment Recommendations based on FDA labeling added a key under the table</li> <li>▪ In Table 8: Treatment Recommendations based on FDA labeling added FDA approved indications, Genotype, Treatment, FDA Labeled dose, and Treatment Duration for Vosevi.</li> <li>▪ In Contraindications chart added Vosevi.</li> </ul>
	References updated
08-28-2017	<p>Policy published 09-01-2017. Policy retro-effective to 08-28-2017.</p> <p>In Description section:</p> <ul style="list-style-type: none"> <li>▪ Added New to Market Hepatitis C Target Agent of Mavyret (glecaprevir/pibrentasvir)</li> <li>▪ Added Mavyret to the FDA Approved Indications and Dosage chart</li> </ul> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Table 8: Treatment Recommendations based on FDA labeling added FDA approved indications, Genotype, Treatment, FDA Labeled dose, and Treatment Duration for Mavyret.</li> <li>▪ In Contraindications chart added Mavyret.</li> </ul>
	References updated

<b>REVISIONS</b>	
10-15-2017	<p>Policy posted 10-27-2017. Policy retro-effective to 10-25-2017.</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Table 2: Harvoni Treatment Recommendations based on FDA Labeling added "are not black or African-American" to read "Treatment-naïve with initial viral load of &lt;6 M IU/mL and without cirrhosis, HIV infection, history of liver transplantation, and/or are not black or African-American"</li> </ul> <p>Rationale section updated</p> <p>References updated</p>
11-15-2017	<p>Policy published 11-21-2017. Policy retro-effective to 11-15-2017.</p> <p>Description section updated</p> <ul style="list-style-type: none"> <li>▪ In the Target Drugs Chart, Mavyret (glecaprevir/pibrentasvir) and Vosevi (sofosbuvir / velpatasvir / voxilaprevir) were moved from the Net to Market Hepatitis C Target Agents to the Preferred Agents.</li> <li>▪ In the Target Drugs Chart, with Mavyret and Vosevi now preferred agents, this means Eplusa, Harvoni, Mavyret, and Vosevi are now co-preferred for the genotypes</li> </ul> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item B Harvoni, removed "ii. The previous treatment is Sovaldi and ribavirin with or without peg-interferon and the patient has BOTH of the following: <ol style="list-style-type: none"> <li>1) Genotype 1 AND</li> <li>2) Cirrhosis"</li> </ol> </li> <li>▪ In Item B Harvoni Length of Approval replaced "Tables 2, 3, and 4" with "Tables 2 and/or 3." Removed "Table 4: Harvoni Treatment Recommendations based on AASLD/IDSA Guidelines"</li> <li>▪ In Item C added dedicated criteria for Mavyret "C. Mavyret will be approved when ALL of the following criteria are met: <ol style="list-style-type: none"> <li>1. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 AND</li> <li>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</li> <li>3. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND</li> <li>4. The patient does not have any FDA labeled contraindications to the requested agent AND</li> <li>5. The patient has not been previously treated with the requested agent AND</li> <li>6. The dose is within the FDA labeled dose AND</li> <li>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 4 (FDA labeling)</li> </ol> Length of approval: Up to the duration of treatment as determined in Table 4." </li> <li>▪ Added "Table 4: Mavyret Treatment Recommendations based on FDA labeling"</li> <li>▪ In Item G added dedicated criteria for Vosevi "F. Vosevi will be approved when ALL of the following criteria are met: <ol style="list-style-type: none"> <li>1. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 AND</li> <li>2. If genotype 1, the prescriber has provided the patient's subtype AND</li> <li>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</li> <li>4. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND</li> <li>5. The patient does not have any FDA labeled contraindications to the requested agent AND</li> <li>6. BOTH of the following: <ol style="list-style-type: none"> <li>a. The patient is not treatment naïve AND</li> <li>b. The patient has not been previously treated with the requested agent AND</li> </ol> </li> <li>7. The dose is within the FDA labeled dose AND</li> <li>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)</li> </ol> Length of approval: Up to the duration of treatment as determined in Table 7." </li> <li>▪ Added "Table 7: Vosevi Treatment Recommendations based on FDA labeling"</li> <li>▪ In Table 9: Treatment Recommendations based on FDA labeling removed Mavyret and Vosevi criteria. (Note Table is left blank as there are currently no new to market drugs without dedicated criteria.)</li> </ul>

<b>REVISIONS</b>	
	<ul style="list-style-type: none"> <li>▪ In Item I removed "3. If requesting Zepatier, the patient has severe renal impairment (i.e. stage 4 or 5 Chronic Kidney disease as indicated by eGFR of &lt;30 mL/min/1.73 m2) or end stage renal disease requiring hemodialysis"</li> <li>▪ In Contraindications chart for Mavyret replaced "and" with "or" to read "Patients with severe hepatic impairment (Child-Pugh C) Coadministration with atazanavir or and rifampin"</li> </ul>
	Rationale section updated
	References updated
10-01-2018	<p>In Description section:</p> <ul style="list-style-type: none"> <li>▪ Revised Preferred and Non-Preferred Agents into chart instead of list for more clarity</li> <li>▪ Updated FDA Approved Indications and Dosage chart</li> </ul> <p>In Policy section:</p> <div style="border: 1px solid black; padding: 5px;"> <p>Summary of revisions:</p> <ul style="list-style-type: none"> <li>• Separated out screening for HBV and monitoring for flare-up or reactivation into 2 bullet points. Both requesting prescribers and the pharmacist reviewers were getting confused on this requirement</li> </ul> </div> <ul style="list-style-type: none"> <li>▪ In Eplclusa Item 2, Harvoni Item 3, and Mavyret Item 2, Technivie Item 2, Viekira Pak and Viekira XR Item 3, Vosevi Item 3, Zepatier Item 3, and New To Market Chronic Hepatitis C Agents Evaluation Item 2 B i removed "will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent" and created new item to read "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"</li> <li>▪ In Technivie Item 1, Viekira Pak and Viekira XR Item 3, and Zepatier Item 1 removed "compensated" to read "The patient has a diagnosis of chronic hepatitis C..."</li> <li>▪ Updated Contraindications chart</li> </ul>
	Rationale section updated
	References updated
12-17-2018	Policy published 01-01-2019. Policy retro-effective to 12-17-2018.
	Description section updated to note generic availability of Harvoni and Eplclusa, Ledipasvir/Sofosbuvir and Sofosbuvir/Velpatasvir as a target agent
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In the Eplclusa section added "or Sofosbuvir/Velpatasvir" to read "Eplclusa or Sofosbuvir/Velpatasvir will be approved..."</li> <li>▪ In the Harvoni section added "or Ledipavir/Sofosbuvir" to read "Harvoni or Ledipavir/Sofosbuvir will be approved..."</li> </ul>

## **REFERENCES**

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2. Technivie prescribing information. Abbvie Inc. November 2017.
3. Viekira prescribing information. Abbvie Inc. November 2017.
4. Zepatier prescribing information. Merck. February 2017.
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7. Eplclusa prescribing information. Gilead. November 2017.
8. Viekira XR prescribing information. Abbvie.. November 2017
9. 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> Accessed November 2016.
10. Vosevi prescribing information. Gilead. November 2017.
11. Mavyret prescribing information. AbbVie. December 2017.