Medical Policy

BlueCross BlueShield of Kansas
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Title: Hepatitis C Second Generation Antivirals – Through Preferred Agent(s)

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

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

Prior Authorization Form:
https://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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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 and/or clinical studies. If the client has preferred agent(s), a preferred agent may be approved for use once all criteria have been met; a non-preferred agent may be approved if the patient is currently treated with the non-preferred agent or the prescriber has provided documentation in support of use of non-preferred agent over the preferred agent.

Target Drugs

Preferred Agents	Non-Preferred Agents
▪ **Epclusa**® (sofosbuvir/velpatasvir) (co-preferred for genotype 1, 2, 3, 4, 5, and 6) ▪ **Harvoni®** (ledipasvir / sofosbuvir) (co-preferred for genotype 1, 4, 5, and 6) ▪ **Mavyret**™ (glecaprevir/pibrentasvir) (co-preferred for genotype 1, 2, 3, 4, 5, and 6) ▪ **Vosevi**™ (sofosbuvir / velpatasvir / voxilaprevir) (co-preferred for genotype 1, 2, 3, 4, 5, and 6)	▪ **Technivie**™ (ombitasvir/paritaprevir/ritonavir) ▪ **Viekira Pak**™ (ombitasvir/paritaprevir/ritonavir + dasabuvir) ▪ **Viekira XR**™ (dasabuvir/ombitasvir/paritaprevir/ritonavir) ▪ **Zepatier**™ (elbasvir/grazoprevir)

FDA Approved Indications and Dosage [1,2,3,4,7,8, 10,11]

Medication	Indications	Dose and Interval
Epclusa (sofosbuvir/ velpatasvir)	Treatment of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection: ▪ without cirrhosis or with compensated cirrhosis ▪ with decompensated cirrhosis (use in combination with ribavirin)	1 tablet orally once daily containing 400 mg of sofosbuvir and 100 mg of velpatasvir for 12 weeks
Harvoni (ledipasvir-sofosbuvir)	Treatment, with or without ribavirin, of adults with chronic hepatitis C, genotype 1, 4, 5, or 6 infection Treatment of pediatric patients 12 years of age or older or weighing at least 35 kg with chronic hepatitis C, genotype 1, 4, 5, or 6 without or with compensated cirrhosis	1 tablet orally once daily containing 90 mg of ledipasvir and 400 mg of sofosbuvir for up to 24 weeks
Mavyret (glecaprevir/pibrentasvir)	Treatment of adult patients within chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child Pugh A) Treatment of adult patients within chronic hepatitis C 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	3 tablets orally once daily for up to 16 weeks

Medication	Indications	Dose and Interval
Technivie (ombitasvir/ paritaprevir/ ritonavir)	Treatment, in combination with ribavirin, of chronic hepatitis C genotype 4 without cirrhosis or with compensated cirrhosis	Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) for 12 weeks
Viekira Pak (paritaprevir/ ritonavir/ ombitasvir and dasabuvir)	Treatment of adult patients, with chronic hepatitis C virus: genotype 1b with or without compensated cirrhosis ▪ genotype 1a with or without compensated cirrhosis. Use in combination with ribavirin for genotype 1a	Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) and one dasabuvir 250 mg tablet twice daily (morning and evening) for up to 24 weeks.
Viekira XR (paritaprevir/ ritonavir/ ombitasvir and dasabuvir)	Treatment of adult patients with chronic hepatitis C virus: ▪ genotype 1b with or without compensated cirrhosis ▪ genotype 1a with or without compensated cirrhosis. Use in combination with ribavirin for genotype 1a	3 tablets taken once daily for up to 24 weeks
Vosevi (sofosbuvir/ velpatasvir/ voxilaprevir)	Treatment of adult patients with HCV infection without cirrhosis or compensated cirrhosis (Child-Pugh A) who have: ▪ genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor ▪ genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor	1 tablet taken once daily for 12 weeks
Zepatier (elbasvir/ grazoprevir)	Treatment, with or without ribavirin, of chronic hepatitis C genotype 1 or 4 infection	1 tablet (50 mg elbasvir and 100 mg grazoprevir) once daily for up to 16 weeks

POLICY

Prior Authorization Criteria for Approval

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

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

Table 1: Epclusa Treatment Recommendations based on FDA labeling

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

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

Prior Authorization Criteria for Approval

B. **Harvoni** will be approved when ALL of the following criteria are met:

1. The patient has a diagnosis of chronic hepatitis C genotype 1, 4, 5, or 6
   AND
2. The prescriber has provided the patient's baseline HCV RNA level if the patient has genotype 1
   AND
3. The prescriber has screened the patient for current or prior hepatitis B viral (HBV) infection and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
   AND
4. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist
   AND
5. The patient does not have any FDA labeled contraindications to the requested agent
   AND
6. ONE of the following:
   a. The patient is treatment naïve
      OR
   b. The patient was previously treated (i.e. treatment experienced) with 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 ~~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 ^	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†
	Treatment-experienced** with compensated cirrhosis (Child-Pugh A) and ineligible for ribavirin £	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^	Treatment	Treatment Duration
1	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)	Harvoni	24 weeks
4, 5, or 6	Treatment-naïve and treatment experienced¥, without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks

^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.
† Harvoni + ribavirin for 12 weeks can be considered in treatment-experienced HCV genotype 1 patients with cirrhosis who are eligible for ribavirin. For this patient population Prime will require treatment with Harvoni in combination with ribavirin for 12 weeks unless the patient is ineligible to receive ribavirin.
£Ribavirin ineligible - patients with history of intolerance, contraindication, or hypersensitivity to ribavirin
¥Treatment-experienced patients who have failed an interferon based regimen with or without ribavirin

Prior Authorization Criteria for Approval

C. **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 will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
   AND
3. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist
   AND
4. The patient does not have any FDA labeled contraindications to the requested agent
   AND
5. The patient has not been previously treated with the requested agent
   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 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[1] 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[2] but without prior treatment with an NS5A inhibitor	Mavyret	12 weeks	12 weeks
1, 2, 4, 5, or 6	Treatment experienced with PRS[3]	Mavyret	8 weeks	12 weeks
3	Treatment experienced with PRS[3]	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.

Prior Authorization Criteria for Approval

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

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

Table 5: Technivie Treatment Recommendations based on FDA labeling

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

Prior Authorization Criteria for Approval

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

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

Patient Population	Treatment*	Treatment Duration
Genotype 1b, with or without compensated cirrhosis	Viekira PAK OR Viekira XR	12 weeks
Genotype 1a or 1b, post liver transplant with normal hepatic function (i.e. Metavir ≤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.

Prior Authorization Criteria for Approval

F. **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 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. 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
   7. The dose is within the FDA labeled dose
      AND
   8. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype as noted in Table 7 (FDA labeling)

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

Table 7: **Vosevi Treatment Recommendations based on FDA labeling**

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

Prior Authorization Criteria for Approval

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

8. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype as noted in Table 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 ^ £	Treatment	Duration
Genotype 1a: Treatment-naïve or PegIFN/RBV-experienced without baseline NS5A polymorphisms†	Zepatier	12 weeks
Genotype 1a: Treatment-naïve or PegIFN/RBV-experienced with baseline NS5A polymorphisms†	Zepatier + ribavirin	16 weeks
Genotype 1b: Treatment-naïve or PegIFN/RBV-experienced	Zepatier	12 weeks
Genotype 1a or 1b: PegIFN/RBV/protease inhibitor-experienced	Zepatier + ribavirin	12 weeks
Genotype 4: Treatment-naive	Zepatier	12 weeks
Genotype 4: PegIFN/RBV-experienced	Zepatier + ribavirin	16 weeks

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

Prior Authorization Criteria for Approval

H. **New to market chronic Hepatitis C agents** will be approved when ALL of the following criteria are met:
   1. The patient has an FDA approved diagnosis for the requested agent
      AND
   2. BOTH of the following:
      a. FDA labeling for the requested agent requires patients are tested for hepatitis B viral (HBV) infection prior to starting treatment with the requested agent
         AND
      b. The prescriber has screened the patient for current or prior HBV and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent
      AND
   3. The requested agent is FDA approved for treatment of the patient's genotype
      AND
   4. The patient does not have any FDA labeled contraindications to the requested agent
      AND

5. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist
   AND
6. The dose is within the FDA labeled dose
   AND
7. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's diagnosis and genotype as noted in Table 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

Prior Authorization Criteria for Approval

I. ***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)
Epclusa (sofosbuvir/velpatasvir)	▪ Epclusa and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated
Harvoni (ledipasvir/sofosbuvir)	▪ If used in combination with ribavirin, all contraindications to ribavirin also apply to Harvoni combination therapy.
Mavyret (glecaprevir/pibrentasvir)	▪ Patients with severe hepatic impairment (Child-Pugh C) Coadministration with atazanavir or rifampin
Technivie (ombitasvir/paritaprevir/ ritonavir)	▪ Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)]. ▪ Co-administration with drugs that are: highly dependent on CYP3A for clearance; moderate and strong inducers of CYP3A. ▪ Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Steven-Johnson syndrome). ▪ The contraindications to ribavirin also apply to this combination regimen (Technivie + ribavirin).

Agent(s)	Contraindication(s)
Viekira Pak (ombitasvir/paritaprevir/ritonavir + dasabuvir) and **Viekira XR** (dasabuvir/ombitasvir paritaprevir/ritonavir)	▪ Patients with moderate to severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)]. ▪ Known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Steven-Johnson syndrome). ▪ Co-administration with drugs that are: highly dependent on CYP3A for clearance; moderate or strong inducers of CYP3A and strong inducers of CYP2C8; and strong inhibitors of CYP2C8. ▪ If Viekira PAK or Viekira XR is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen.
Vosevi (sofosbuvir/velpatasvir/ voxilaprevir)	▪ Coadministration with rifampin
Zepatier (elbasvir/grazoprevir)	▪ Patients with moderate or severe hepatic impairment [decompensated cirrhosis (Child-Pugh B or C)]. ▪ Organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors, strong CYP3A inducers, and efavirenz. ▪ If Zepatier is administered with ribavirin, the contraindications to ribavirin also apply.

RATIONALE

Disease Background[5,6]

Hepatitis C is an infection of the liver caused by the Hepatitis C virus (HCV) and is one of the leading causes of chronic liver disease in the United States. According to the Centers for Disease Control and Prevention (CDC), there were an estimated 3.5 million people infected with hepatitis C as of 2015. Hepatitis C infection can either be acute or chronic. Acute HCV infection is defined as presenting within 6 months following exposure to the virus. The infection is defined as chronic if the virus is present beyond 6 months following exposure. 70% to 80% of those infected with HCV will go on to develop chronic HCV infection.

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

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

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

AASLD/IDSA guidelines on when and in whom to treat: [5]
The goal of therapy is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure. According to the AASLD/IDSA guidelines, treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Treatment should be initiated early because delaying therapy may decrease the benefits of eradicating the hepatitis C viral infection.

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

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

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

Efficacy of this combination in treatment naïve patients with HCV genotype 1 with or without cirrhosis was evaluated in the C-EDGE TN and C-EDGE COINFECTION trials. Subjects in both trials received elbasvir/grazoprevir for 12 weeks. SVR12 was 95% in both trials. There were no significant differences in SVR12 between cirrhotic and non-cirrhotic patients. The C-EDGE TE trial evaluated efficacy of this combination in treatment experienced HCV genotype 1 patients with or without cirrhosis who had previously failed peginterferon plus ribavirin. Subjects received elbasvir/grazoprevir monotherapy for 12 weeks or elbasvir/grazoprevir with ribavirin for 16 weeks. SVR12 rates in the two treatment groups were 94% and 97% respectively. Efficacy in HCV genotype 1 patients with or without cirrhosis who had previously failed peginterferon, ribavirin, plus a protease inhibitor was evaluated in the C-SALVAGE trial. This was an open label, single arm trial. All subjects received elbasvir/grazoprevir plus ribavirin for 12 weeks. Overall SVR12 was 96%.

Efficacy of this combination in patients with HCV genotype 1 with or without cirrhosis and who had Chronic Kidney Disease (CKD) stage 4 (eGFR 15-29 mL/min/1.73 m^2) or CKD Stage 5 (eGFR <15 mL/min/1.73 m^2), including patients on hemodialysis was evaluated in the C-SURFER trial. Patients were randomized to receive either elbasvir/grazoprevir for 12 weeks or placebo for 12 weeks followed by 12 weeks of elbasvir/grazoprevir (deferred treatment group). Overal SVR12 was 99%. There were no significant differences with regard to safety in the elbasvir/grazoprevir group versus placebo group.

These trials found that presence of NS5A amino acid polymorphisms in patients with HCV genotype 1a was associated with reduced efficacy of elbasvir/grazoprevir regardless of treatment

history or cirrhosis status. It is recommended to test for NS5A polymorphisms in HCV genotype 1a patients prior to starting treatment with this combination. If the polymorphism is present, addition of ribavirin to the treatment regimen and extension of the duration of treatment to 16 weeks is recommended.

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

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

Glecaprevir/pibrentasvir[11]

Glecaprevir/pibrentasvir is a combination of an NS3/4A protease inhibitor and an NS5A inhibitor. Its safety and efficacy have been demonstrated in treatment naïve patients 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 glecaprevir/pibrentasvir.

The most common adverse events associated with glecaprevir/pibrentasvir are headache and fatigue.

Ledipasvir-sofosbuvir[1]

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

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

Ombitasvir/paritaprevir/ritonavir and dasabuvir [3]
Safety and efficacy of this combination was evaluated in 4 pivotal trials including treatment naïve, previous failures, cirrhotics and non-cirrhotic genotype 1 patients. The studies (Sapphire I, Turquoise II, Pearl III and Pearl IV) all had a primary efficacy endpoint of a sustained virologic response (SVR) at 12 weeks after the end of therapy. Sapphire I was conducted in treatment naïve patients without cirrhosis. Turquoise-2 was conducted in treatment naïve and previously treated patients and included cirrhotic patients. Pearl III evaluated treatment naïve genotype 1b patients and Pearl IV evaluated treatment naïve genotype 1a patients. SVR rates in these trials ranged from 90% to 99%. Treatment guidelines recommend that patients that have failed a previous protease inhibitor containing regimen receive ledipasvir/sofosbuvir. Ombitasvir/paritaprevir/ritonavir + dasabuvir is not a recommended regimen in previous protease inhibitor failures due to risk of resistance.

Ombitasvir/paritaprevir/ritonavir[2]
Efficacy and safety of this combination, when used with or without ribavirin, was evaluated in a single clinical trial (PEARL-I). The study enrolled 135 subjects with chronic hepatitis C (HCV) infection genotype 4 without cirrhosis. The subjects were either treatment naïve or had history of virologic failure following treatment with pegylated interferon and ribavirin. The primary end point of the study was sustained virologic response at 12 weeks (SVR 12) following completion of therapy. SVR 12 was 100% for treatment naïve and treatment experienced subjects whose regimen included ribavirin and 91% for treatment naïve patients whose regimen did not include ribavirin. Safety and efficacy of this combination regimen has not been studied in patients previously treated with a direct acting antiviral.

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

Sofosbuvir/velpatasvir[7]
Efficacy of this combination agent was evaluated in four phase 3 trials (ASTRAL-1, ASTRAL-2, ASTRAL-3, and ASTRAL-4). All these trials included patients who were either treatment naïve or had previously been treated with an interferon based regimen (peginterferon plus ribavirin with or without a protease inhibitor). The primary endpoint for these trials was sustained virologic response at 12 weeks (SVR 12) following completion of therapy. ASTRAL-1 was a placebo controlled trial that enrolled patients with HCV infection genotype 1, 2, 4, 5, or 6. Overall, the SVR 12 rate was 99% in patients who received sofosbuvir/velpatasvir and 0% in those receiving placebo (95% confidence interval, $p<0.001$) . ASTRAL-2 and ASRTAL-3 were randomized, open label trials evaluating efficacy in patients with HCV genotype 2 or 3 respectively. Those with HCV genotype 2 received either sofosbuvir/velpatasvir for 12 weeks or sofosbuvir plus ribavirin for 12 weeks. The SVR12 rates for the two treatment arms were 99% and 94% respectively. Subjects with HCV genotype 3 were randomized to receive either sofosbuvir/velpatasvir for 12 weeks or sofosbuvir plus ribavirin for 24 weeks. The SVR 12 rates were 95% and 80% respectively. ASTRAL-4 was an open label trial that evaluated efficacy of sofosbuvir/velpatasvir in patients with decompensated cirrhosis. Patients were randomized to receive one of three treatment regimens: sofosbuvir/velpatasvir for 12 weeks, sofosbuvir/velpatasvir for 24 weeks, or sofosbuvir/velpatasvir plus ribavirin for 12 weeks. SVR 12 rates were 83%, 86%, and 94% respectively.

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

Sofosbuvir/velpatasvir/voxilaprevir[10]
Sofosbuvir/velpatasvir/voxilaprevir is a fixed-dose combination of sofosbuvir, a nucleotide analog NS5B polymerase inhibitor, velpatasvir, an HCV NS5A inhibitor, and voxilaprevir, an HCV NS3/4A protease inhibitor. Efficacy of this combination agent has been demonstrated in patients with HCV genotype 1, 2, 3, 4, 5, or 6 who have previously been treated with a regimen containing an NS5A inhibitor and in patients with genotype 1a or 3 infection who have been previously treated with a regimen containing sofosbuvir without an NS5A inhibitor. 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.

The most common adverse events reported in patients who received sofosbuvir/velpatasvir/voxilaprevir were headache, fatigue, diarrhea, and nausea.

Risk of Hepatitis B infection reactivation with HCV Direct Acting Antivirals[9]
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.

REVISIONS	
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: ▪ Added Harvoni to read "(Harvoni [ledipasvir/sofosbuvir]… "
	In Description section: ▪ Added Harvoni to Target Drugs ▪ Updated FDA Approved Indications and Dosage chart.
	In Policy section: ▪ In Item A added "Harvoni" to read " "Harvoni (ledipasvir/sofosbuvir and paritaprevir/ritonavir/ombitasvir + dasabuvir will be approved when the following criteria are met:" ▪ 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" ▪ In Item A added "Table 1 Harvoi Treatment Duration Recommendations" ▪ 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"
	Coding section removed as codes are not used for pharmacy benefit.
	References updated
02-24-2015	▪ 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)

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	(Harvoni [ledipasvir/sofosbuvir], paritaprevir/ritonavir/ombitasvir + dasabuvir, and Sovaldi [sofosbuvir])" ▪ Related policy titles added under title.
	Description section updated
	In Policy section: ▪ 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:" ▪ 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" 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)" ▪ In new Item 2 added "If able, the prescriber will provide an SVR post treatment week 12." ▪ In Item 4 added a Contraindications chart. ▪ Added Item 8 "If the request is for Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir) ALL of the following: a. The patient has not been previously treated with a regimen containing sofosbuvir, simeprevir, telaprevir, or boceprevir b. The patient's subtype has been identified and provided c. The patient does not have decompensated liver disease OR ▪ Added Item 9 If the request is for Harvoni, the following: a. The patient has not been previously treated with Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir) AND b. ONE of: i. The patient has NOT failed a previous sofosbuvir containing regimen OR ii. BOTH of the following: 1. The patient has failed a previous sofosbuvir containing regimen AND 2. The patient has advanced fibrosis (Metavir F3 or F4) ▪ In Item 10 move "25 mg ombitasavir" to another location within the statement. ▪ Updated Table 1 to indicated "Treatment naïve without cirrhosis and initial viral load < 6 M IU/mL" is "8 weeks" ▪ Added Table 2 reflecting "Viekira Treatment Duration Recommendations based on labeling" and "Length of Approval" ▪ Removed all criteria and Length of Approval for "Initial Evaluation Sovaldi (sofosbuvir ± Pegylated Interferon ± Olysio" "1. The patient is naïve to therapy with Sovaldi AND 2. The agent is being prescribed by a specialist or in consultation with a specialist (i.e. Gastroenterologist, Hepatologist, Infectious Disease) AND 3. The patient has a diagnosis of chronic hepatitis C infection confirmed by serological markers AND 4. Sofosbuvir will be used in a combination antiviral treatment regimen supported by FDA approved labeling or the AASLD guidelines (listed in Rationale below) a. If genotype 1, treatment naïve requesting the combination of simeprevir and sofosbuvir, the patient has BOTH of the following: i. a METAVIR score of 3 or 4 AND ii. Ineligible to receive peginterferon AND 5. The patient does NOT have any FDA labeled contraindications to sofosbuvir or the other agents used in the combination therapy AND 6. The patient will NOT be receiving Incivek (telaprevir) or Victrelis (boceprevir) concomitantly with sofosbuvir AND 7. The patient is not coinfected with chronic hepatitis B AND 8. If the patient has hepatocellular carcinoma the following are met: a. 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 b. The patient has NO extrahepatic manifestations of cancer or evidence of vascular invasion of tumor AND

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	9. The dosing of sofosbuvir is within the FDA labeled dosage (400 mg daily) AND 10. If the treatment regimen includes simeprevir, the dosing of simeprevir is within the FDA labeled dosage (150 mg daily)" "Length of approval: As determined below in Table 3 for Sovaldi containing regimens based on regimen and genotype" ▪ Removed all criteria and Length of Approval for "Nonpreferred Agent(s) peginterferon (TRIPLE THERAPY)" "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 is met: 1. The patient is currently being treated with the non-preferred agent OR 2. The patient has a history of a trial of the preferred peginterferon OR 3. The patient has an FDA labeled contraindication, documented intolerance, or hypersensitivity to the preferred agent(s) peginterferon OR 4. The prescriber has submitted documentation in support of the use of the non-preferred agent(s) peginterferon, for the intended diagnosis" "Length of approval: Up to 48 weeks based on regimen" Removed related tables of "AASLD Supported Sovaldi® Containing Antiviral Regimens", "IFN ineligible definitions", and "Approval Durations"
	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: ▪ In Item A added Viekira Pak genetic drug names "(ombitasvir / paritaprevir / ritonavir + dasabuvir)" ▪ 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" ▪ In Item A 8 d added "esophageal varices" to read "(e.g. portal hypertension, esophageal varices)" ▪ 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" ▪ In Item 10 added "ALL of" to read "If the request is for Harvoni, ALL of the following:" ▪ 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)" ▪ 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)" ▪ Updated the Harvoni Treatment Duration Recommendations table. ▪ Added: "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. The prescriber has submitted documentation in support of the use of the non-preferred agent(s), for the intended diagnosis."
	Rationale section updated
	References updated
01-01-2016	Policy published 12-30-2015. Policy effective 01-01-2016.
	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™)"
	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 PakTM [ombitasvir/paritaprevir/ritonavir + dasabuvir])" And

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	"II.2015 Hepatitis C Second Generation Antivirals PA (TechnivieTM [ombitasvir/ paritaprevir/ritonavir])" Rationale and References sections remain combined
	In I. 2015 Hepatitis C Second Generation Antivirals PA Description section: ▪ Updated Description ▪ In Target Drugs Chart moved Viekira Pak from being a Preferred Agent to being a Non-Preferred Agent
	▪ In I. 2015 Hepatitis C Second Generation Antivirals PA Policy section: ▪ In Item 1 removed "genotype 1" to read "The patient has a diagnosis of chronic hepatitis C, confirmed by serological markers" ▪ In Item 9 added "a. The patient has chronic hepatitis C genotype 1" ▪ 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" ▪ In Item 10 removed "ALL" and added "ONE" to read, "If the request is for Harvoni, ONE of the following:" ▪ In Item 10 a added "i. The patient has chronic hepatitis C genotype 1" ▪ 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)" ▪ 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)" ▪ In Table 1 Harvoni Treatment Duration Recommendations added Patient Population and Treatment Duration for Genotype 4, 5, and 6
	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
	In II.2015 Hepatitis C Second Generation Antivirals PA Policy section: ▪ Added new policy information of "Initial 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 confirmed by serological markers AND 2. 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) AND 3. The requested agent is being prescribed by a specialist (i.e. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND 4. The requested agent will be used in a combination antiviral treatment regimen supported by FDA approved labeling (see Table 1 below) AND 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 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 7. The patient does not have Hepatocellular Carcinoma (HCC) AND 8. The patient is not co-infected with Hepatitis B virus (HBV) AND 9. ONE of the following:

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	a. The patient has a METAVIR score of 2 or 3 OR b. The patient has a Ishak score of 3 to 5 OR c. The patient has a Fibroscan score of 7.65 kPa to 13.00 kPa OR d. The patient is post-liver transplant OR e. The patient is co-infected with HIV-1 AND 10. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent AND 11. The dose is within the FDA labeled dose (25 mg ombitasvir/150 mg of paritaprevir/100 mg ritonavir) Length of Approval: Up to 12 weeks as determined by Table 1" ▪ Added Technivie Treatment Duration Recommendations based on FDA labeling and Contraindications charts. ▪ Added the Non-preferred policy language 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. 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
	Updated Rationale section
	Updated References
03-21-2016	Removed from title the wording "(2015)" and "(Harvoni®, Viekira™, Technivie™) to read "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s)"
	In Section I Hepatitis C Second Generation Antivirals PA - Through Preferred Oral agent(s)
	Description section updated
	Updated Target Drugs–Non-Preferred Agent adding Zepatier
	Updated FDA Approved Indications and Dosage chart to include adding Zepatier (elbasvir/grazoprevir)
	In Policy section: ▪ In Initial Evaluation Header added "Zepatier" and removed "(ombitasvir / paritaprevir / ritonavir + dasabuvir)" ▪ 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." ▪ In Item 5 added Zepatier to the contraindications chart. ▪ 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" ▪ In Item 9 b added "elbasvir, grazoprevir" ▪ In Item 10 added "(ledipasvir/sofosbuvir)" to read "Harvoni (ledipasvir/sofosbuvir)" ▪ 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)" ▪ 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)" ▪ 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 (daclatasvir), Harvoni (ledipasvir/sofosbuvir), Sovaldi (sofosbuvir), Technivie (ombitasvir/paritaprevir/ritonavir), Viekira (ombitasvir/paritaprevir/ritonavir + dasabuvir), or Zepatier (elbasvir/grazoprevir)" ▪ Added "11. 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 AND

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	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" 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)" ▪ In Length of Approval added "and 3 below" to read "Up to 24 weeks as determined in Tables 1, 2, and 3 below." ▪ Updated Table 1 Harvoni Treatment Duration Recommendations based on FDA Labeling and Table 2 Viekira Treatment Duration Recommendations based on FDA labeling ▪ Added Table 3 Zepatier Treatment Duration Recommendations based on FDA labeling ▪ 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 <30 mL/min/1.73 m2) or end stage renal disease requiring hemodialysis OR"
	In Section II Hepatitis C Second Generation Antivirals PA
	Updated FDA Approved Indications and Dosage chart
	▪ In Policy section: ▪ 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." ▪ 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)" ▪ 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)"
	Updated Rationale section
	Updated References
06-01-2016	Published 05-25-2016. Effective 06-01-2016.
	I. Initial Evaluation - Harvoni, Viekira Pak, and Zepatier Policy section: ▪ In Item 2 added "If requesting Harvoni" to read "If requesting Harvoni, the prescriber has provided a baseline HCV RNA level" ▪ Removed the following criteria: "ONE of the following: a. The patient has a METAVIR score of ≥2 OR b. The patient has a Ishak score ≥3 OR c. The patient has a Fibroscan score of ≥7.65 kPa OR d. The patient has radiological imaging consistent with fibrosis and/or cirrhosis (e.g. portal hypertension, esophageal varices) OR e. The patient has type 2 or 3 mixed cryoglobulinemia with end-organ manifestations (e.g. vasculitis) OR f. The patient has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis OR g. The patient is currently awaiting liver transplant OR h. The patient is post-liver transplant OR i. The patient is co-infected with HIV-1"
	II. Technivie Description section updated
	II. Technivie Policy section ▪ Removed the following criteria: "ONE of the following: a. The patient has a METAVIR score of ≥2 OR b. The patient has a Ishak score ≥3 OR c. The patient has a Fibroscan score of ≥7.65 kPa OR d. The patient has radiological imaging consistent with fibrosis and/or cirrhosis (e.g. portal hypertension, esophageal varices) OR e. The patient has type 2 or 3 mixed cryoglobulinemia with end-organ manifestations (e.g. vasculitis) OR f. The patient has proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis OR g. The patient is currently awaiting liver transplant OR h. The patient is post-liver transplant OR

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	i. The patient is co-infected with HIV-1"
	Added III. Hepatitis C Second Generation New To Market Antivirals 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"
	Rationale section updated to include updating the AASLD recommendations removing priority treatment criteria.
06-01-2016	Published 06-08-2016. Retro-effective to 06-01-2016. ▪ Corrected Revision section (06-01-2016 above) to include the addition of III. Hepatitis C Second Generation New To Market Antivirals
07-25-2016	Published 08-04-2016. Retro-effective to 07-25-2016.
	In III. Hepatitis C Second Generation New To Market Antivirals Description section ▪ Added Epclusa (sofosbuvir/velpatasvir) as a Non-preferred drug ▪ Updated FDA Approved Indications and Dosage chart for Epclusa
	In Policy section: ▪ Updated Treatment Duration Recommendations based on FDA labeling and Contraindications charts for Epclusa
	References updated
09-01-2016	Title changed to "Hepatitis C Second Generation – Through Preferred Agent(s)" from "Hepatitis C Second Generation Antivirals – Through Preferred Oral Agent(s)"
	Description section updated
	In Policy section: ▪ 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:" ▪ 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" ▪ 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" ▪ 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)" ▪ Added Item A 5 "ONE of the following: a. The patient is treatment naïve OR b. The patient was previously treated (i.e. treatment experienced) with ONLY ONE of the following regimens: i. The previous treatment is peg-interferon and ribavirin with or without an HCV protease inhibitor OR ii. The previous treatment is Sovaldi and ribavirin with or without peg-interferon and the patient has BOTH of the following: 1) Genotype 1 AND 2) Cirrhosis" ▪ 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

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	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 ≥5, Fibroscan score ≥ 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 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

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	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 m2) or end stage renal disease requiring hemodialysis OR 4. The prescriber has submitted documentation in support of the use of the non-preferred agent(s), for the intended diagnosis." ▪ 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" ▪ 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:" ▪ In Item F 2 removed "documented intolerance" to read "The patient has an FDA labeled contraindication or hypersensitivity to the preferred agent(s)" ▪ 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 <30 mL/min/1.73 m2) or end stage renal disease requiring hemodialysis" ▪ 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)"

<table>
<tr><td colspan="2"><u>REVISIONS</u></td></tr>
<tr><td></td><td>▪ Contraindications chart updated</td></tr>
<tr><td></td><td>Rationale section updated</td></tr>
<tr><td></td><td>References updated</td></tr>
<tr><td>09-01-2016</td><td>Published 10-12-2016. Retro-effective to 09-01-2016.</td></tr>
<tr><td></td><td>In Description section:
▪ Updated Target Drugs chart to add Viekira XR (ombitasvir/paritaprevir/ritonavir/dasabuvir) as a non-preferred agent.
▪ Updated FDA Approved Indications and Dosage adding Viekira XR (ombitasvir/ paritaprevir/ritonavir/dasabuvir)</td></tr>
<tr><td></td><td>In Policy section:
▪ Updated Table 4 adding “Viekira XR” to read “Viekira PAK and Viekira XR Treatment Recommendations based on FDA labeling” and updated drug combination treatments
▪ Updated Table 6: Treatment Recommendations based on FDA labeling following New to market chronic Hepatitis C agents section adding Epclusa (sofosbuvir/velpatasvir)
▪ Updated the Contraindications chart removing Epclusa (sofosbuvir/velpatasvir) and adding Viekira XR (paritaprevir/ritonavir/ombitasvir/dasabuvir)</td></tr>
<tr><td></td><td>Rationale section updated</td></tr>
<tr><td></td><td>References updated</td></tr>
<tr><td>11-01-2016</td><td>Policy published 11-18-2016. Policy retro-effective to 11-01-2016.</td></tr>
<tr><td></td><td>▪ Description section Target Drugs chart updated moving Epclusa from a Non-Preferred Agent to a Preferred Agent.
▪ FDA Approved Indications and Dosage chart updated</td></tr>
<tr><td></td><td>In Policy section:
▪ Added the following Epclusa criteria and Length of approval chart:
"A. Epclusa will be approved when ALL of the following criteria are met:
1. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 AND
2. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND
3. The patient does not have any FDA labeled contraindications to the requested agent AND
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 with or without an HCV protease inhibitor 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 1 (FDA labeling)
Length of approval: Up to the duration of treatment as determined in Table 1
Table 1: Epclusa Treatment Recommendations based on FDA labeling
<table>
<tr><th>Genotype</th><th>Patient population</th><th>Treatment</th><th>Duration</th></tr>
<tr><td rowspan="2">1, 2, 3, 4, 5, or 6</td><td>Patients without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td><td>Epclusa</td><td>12 weeks</td></tr>
<tr><td>Patients with decompensated cirrhosis (Child-Pugh B and C)</td><td>Epclusa + ribavirin</td><td>12 weeks"</td></tr>
</table>
▪ In Items B, C, D, E, and F updated Table numbers.
▪ Updated Contraindications chart</td></tr>
<tr><td></td><td>Rationale section updated</td></tr>
<tr><td></td><td>References updated</td></tr>
<tr><td>05-15-2017</td><td>In Title section added "Antivirals" to read Hepatitis C Second Generation Antibirals – Through Preferred Agent</td></tr>
<tr><td></td><td>In Description section:
▪ Updated Preferred Agents chart as follows:
✓ To Epclusa added "(preferred for genotype 1, 4, 5, and 6)"
✓ To Harvoni added "(preferred for genotype 2 and 3)"
▪ Updated FDA Approved Indications and Dosage chart for Technivie and Harvoni indications.</td></tr>
<tr><td></td><td>In Policy section:</td></tr>
</table>

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	▪ 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". ▪ In Item B 8 "and 3" to Table listing and revised Table 3 to Table 4. ▪ In Item B Length of Approval added "and 4" to Table listing. ▪ Updated Table 2 ▪ Added new Table 3 and re-numbered Tables accordingly ▪ In Item C revised "Table 4" to "Table 5" ▪ 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" ▪ In Item E revised "Table 6" to "Table 7" ▪ In Item F added "BOTH of the following: a. FDA labeling for the requested agent requires patients are tested for hepatitis B viral (HBV) infection prior to starting treatment with the requested agent AND b. The prescriber has screened the patient for current or prior HBV and will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent" and revised "Table 7" to "Table 8" ▪ Updated Table 5 Technivie Treatment Recommendations based on FDA labeling and Table 6 Viekira PAK and Viekira XR Treatment Recommendations based on FDA labeling.
	Rationale section updated
	References updated
05-15-2017	Published 07-17-2017. Retro-effective to 05-15-2017.
	Corrected wording in the Target Drugs chart to reflect Epclusa (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)".
08-14-2017	Policy published 09-01-2017. Policy retro-effective to 08-14-2017.
	In Description section: ▪ Added New to Market Hepatitis C Target Agent of Vosevi (glecaprevir/pibrentasvir) ▪ Added Vosevi to the FDA Approved Indications and Dosage chart
	In Policy section: ▪ In Table 1: Epclusa Treatment Recommendations based on FDA labeling added a key under the table ▪ In Table 8: Treatment Recommendations based on FDA labeling added FDA approved indications, Genotype, Treatment, FDA Labeled dose, and Treatment Duration for Vosevi. ▪ In Contraindications chart added Vosevi.
	References updated
08-28-2017	Policy published 09-01-2017. Policy retro-effective to 08-28-2017.
	In Description section: ▪ Added New to Market Hepatitis C Target Agent of Mavyret (glecaprevir/pibrentasvir) ▪ Added Mavyret to the FDA Approved Indications and Dosage chart
	In Policy section: ▪ In Table 8: Treatment Recommendations based on FDA labeling added FDA approved indications, Genotype, Treatment, FDA Labeled dose, and Treatment Duration for Mavyret. ▪ In Contraindications chart added Mavyret.
	References updated
10-15-2017	Policy posted 10-27-2017. Policy retro-effective to 10-25-2017.
	In Policy section: ▪ 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 <6 M IU/mL and without cirrhosis, HIV infection, history of liver transplantation, and/or are not black or African-American"
	Rationale section updated
	References updated
11-15-2017	Policy published 11-21-2017. Policy retro-effective to 11-15-2017.
	Description section updated ▪ 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.

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	▪ In the Target Drugs Chart, with Mavyret and Vosevi now preferred agents, this means Epclusa, Harvoni, Mavyret, and Vosevi are now co-preferred for the genotypes
	In Policy section: ▪ 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: 1) Genotype 1 AND 2) Cirrhosis" ▪ 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" ▪ In Item C added dedicated criteria for Mavyret "C. 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 will monitor the patient for HBV flare-up or reactivation during and after treatment with the requested agent AND 3. The requested agent is being prescribed by a specialist (e.g. gastroenterologist, hepatologist, or infectious disease) or in consultation with a specialist AND 4. The patient does not have any FDA labeled contraindications to the requested agent AND 5. The patient has not been previously treated with the requested agent 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 of treatment as determined in Table 4." ▪ Added "Table 4: Mavyret Treatment Recommendations based on FDA labeling" ▪ In Item G added dedicated criteria for Vosevi "F. 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 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. 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 7. The dose is within the FDA labeled dose AND 8. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype as noted in Table 7 (FDA labeling) Length of approval: Up to the duration of treatment as determined in Table 7." ▪ Added "Table 7: Vosevi Treatment Recommendations based on FDA labeling" ▪ 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.) ▪ 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 <30 mL/min/1.73 m2) or end stage renal disease requiring hemodialysis" ▪ 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"
	Rationale section updated
	References updated

REFERENCES

1. Harvoni prescribing information. Gilead. April 2017.
2. Technivie prescribing information. Abbvie Inc. February 2017.
3. Viekira prescribing information. Abbvie Inc. February 2017.
4. Zepatier prescribing information. Merck. February 2017.
5. AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Testing Hepatitis C. Available at www.hcvguidelines.org . Accessed May 2017.
6. The center for Disease Control and Prevention. Viral Hepatitis Statistics and Surveillance. Available at http://www.cdc.gov/hepatitis/statistics . Accessed June 2016.
7. Epclusa prescribing information. Gilead. August 2017.
8. Viekira XR prescribing information. Abbvie. July 2016.
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. July 2017.
11. Mavyret prescribing information. AbbVie. August 2017.