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Section:	Prescription Drugs	**Effective Date:**	January 1, 2019
Subsection:	Anti-Infective Agents	**Original Policy Date:**	December 9, 2016
Subject:	Hepatitis C Agents	**Page:**	1 of 18

Last Review Date: November 30, 2018

Hepatitis C Agents

Description

Epclusa* (sofosbuvir & velpatasvir), **Harvoni*** (ledipasvir & sofosbuvir), **Sovaldi*** (sofosbuvir), **Mavyret*** (glecaprevir and pibrentasvir), **Vosevi*** (sofosbuvir, velpatasvir, & voxilaprevir), Zepatier (elbasvir, grazoprevir)

*Preferred Product

Background

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with hepatitis C virus (HCV) have no symptoms of the disease until liver damage becomes apparent, which may take several years. Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections or liver cancer (1).

Regulatory Status

FDA-approved indications:

1. **Harvoni** is a fixed-dose combination of ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and is indicated for the treatment of chronic hepatitis C (CHC) genotype 1, 4, 5 and 6 infection in adults and children 12 – 17 years of age who are at least 35 kg without cirrhosis or with compensated cirrhosis (2).
2. **Epclusa** is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor, and is

indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infections (3):
    a. Without cirrhosis or with compensated cirrhosis
    b. With decompensated cirrhosis for use in combination with ribavirin
3. **Zepatier** is a fixed-dose combination containing elbasvir, a hepatitis C virus (HCV) NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor, and is indicated with or without ribavirin for treatment of chronic HCV genotypes 1 or 4 infection in adults (4).
4. **Sovaldi** is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen. Sovaldi efficacy has been established in subjects with HCV genotype 1, 2, 3, 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection and in pediatric patients 12 years of age and older and weighing at least 35kg with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin (5).
5. **Ribavirin** is a nucleoside analogue indicated for the treatment of chronic hepatitis C (CHC) virus infection. Ribavirin monotherapy is not effective for the treatment of chronic hepatitis; therefore, Ribavirin capsules must not be used alone (6).
6. **Vosevi** is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, velpatasvir, an HCV NS5A inhibitor, and voxilaprevir, an HCV NS3/4A protease inhibitor, and is indicated for the treatment of adult patients with chronic HCV infection without cirrhosis or with 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. (7)
    a. Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor.
    b. Additional benefit of VOSEVI over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.
7. **Mavyret** is a fixed-dose combination of glecaprevir, a hepatitis C virus (HCV) NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adult patients with chronic HCV genotype (GT) 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A). Mavyret is also indicated for the treatment of adult patients with HCV 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 (8).

No dose recommendation of Harvoni, Epclusa can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30 mL/min/1.73m^2) or with end stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite (2-3).

Vosevi and Zepatier are contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C) due to potential toxicity. Mavyret is not recommended in patients with moderate hepatic impairment (Child-Pugh B) and contraindicated in patients with severe hepatic impairment (Child-Pugh C) due to potential toxicity (4, 7).

If Hepatitis C medication is administered with ribavirin, the contraindications to ribavirin also apply to the combination regimen. The primary toxicity of ribavirin is hemolytic anemia. The boxed warning explains that the anemia associated with ribavirin therapy may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin (6).

There is a boxed warning stating that ribavirin may cause birth defects and fetal death. Therefore, ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of treatment in both female patients and in female partners of male patients who are taking ribavirin therapy. At least two reliable forms of effective contraception must be utilized during treatment and during the 6-month post-treatment follow-up period (6).

All Hepatitis C medications have boxed warning for Hepatitis B virus reactivation, occasionally fulminant, during or after Hepatitis C virus (HCV) therapy which have been reported in HBV/HCV coinfected patients who were not already on HBV suppressive therapy. In light of these observations, all patients initiating HCV therapy should be assessed for HBV coinfection with testing for HBsAg, anti-HBs, and anti-HBc (9).

Drug Interactions:
Harvoni is not recommended in combination with rosuvastatin. Amiodarone is not recommended in combination with Harvoni due to severe bradycardia. Proton pump inhibitors (PPI) can be given with Harvoni but Histamine$_2$ (H_2) blockers preferred (2).

Epclusa is not recommended in combination with rosuvastatin in doses over 10mg. Proton pump inhibitors (PPI) can be given with Harvoni but should be given at least 4 hours apart and Histamine$_2$ (H_2) blockers should be given 12 hours apart (3).

Chronic alcohol use is an important risk factor because alcohol consumption has been associated with more rapid fibrosis progression. Treatment of HCV-infected persons who inject drugs should be delivered in a multidisciplinary care setting with services to reduce the risk of reinfection and for management of the common social and psychiatric comorbidities in this population. Physicians should review alcohol consumption and drug abuse with patients while on hepatitis c medicatuions (9-11).

Safety and effectiveness of Epclusa, Mavyret, Vosevi and Zepatier in children less than 18 years of age have not been established (3-4, 7-8).

Safety and effectiveness of Harvoni and Sovaldi in children less than 12 years of age have not been established (2,5).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Epclusa, Mavyret, Vosevi and Zepatier may be considered **medically necessary** in patients 18 years of age or older with chronic Hepatitis C if the conditions indicated below are met.

Harvoni and Sovaldi may be considered **medically necessary** in patients 12 years of age or older with chronic Hepatitis C if the conditions indicated below are met.

Epclusa, Mavyret, Vosevi and Zepatier are considered i**nvestigational** for patients that are under 18 years of age and for all other indications.

Harvoni and Sovaldi are considered **investigational** for patients that are under 12 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Chronic Hepatitis C
    a. Required documented viral load (HCV RNA) at least 6 months prior to request for treatment)

Harvoni or Epclusa

1. Genotype 1 or 4 with **ONE** of the following:
    a. Treatment-naïve – without cirrhosis
        i. **Harvoni Genotype 1 only** – if the baseline viral load is < 6 million IU/ml, then HCV RNA will be drawn at week 4
    b. Treatment-naïve – with cirrhosis
    c. Treatment-experienced – previously treated with Peg-Interferon and Ribavirin (RBV)
    d. Treatment-experienced – previously treated with Protease Inhibitor (NS3)
        i. Genotype 1 only
        ii. Not indicated for treatment in Genotype 4
    e. Treatment-experienced – previously treated with Sovaldi containing regimen that does NOT include an NS5A inhibitor
        i. Genotype 1 -
            i. Harvoni must be combined with ribavirin
            ii. Epclusa is only recommended for genotype 1b
        ii. Genotype 4 – not indicated for treatment
    f. Decompensated cirrhosis
        i. Genotype 1 – must be combined with Ribavirin (RBV) unless RBV ineligible
        ii. Genotype 4 – must be combined with Ribavirin (RBV) unless RBV ineligible
    g. Post-Transplant
        i. **Harvoni only –** it must be combined with Ribavirin (RBV)
        ii. Epclusa is not recommended in treatment post-transplant
    h. Hepatocellular Carcinoma
        i. Must be combined with Ribavirin (RBV)

2. Genotype 2 or 3 – **Epclusa** only with **ONE** of the following:
    a. Treatment-naïve

b. Treatment-experienced – previously treated with Peg-Interferon and Ribavirin
c. Treatment-experienced – previously treated with Sovaldi and Ribavirin (RBV)
    i. Genotype 3 – **NOT** recommended
d. Decompensated cirrhosis
    i. Must be combined with Ribavirin (RBV)
e. Post-Transplant
    i. Genotypes 2 and 3 with cirrhosis
    ii. Must be combined with ribavirin
f. Hepatocellular Carcinoma
    i. Must be combined with Ribavirin (RBV)

3. Genotype 5 or 6 with **ONE** of the following:
    a. Treatment-naïve
    b. Treatment-experienced – previously treated with Peg-Interferon and Ribavirin (RBV)
    c. Decompensated cirrhosis
    d. Hepatocellular Carcinoma
        i. Must be combined with Ribavirin (RBV)
    e. Post-Transplant
        i. Harvoni only – must be combined with Ribavirin (RBV)

AND the following:

a. Absence of severe renal impairment (eGFR less than 30 ml/min/1.73m^2) or end stage renal disease (ESRD) requiring hemodialysis

Zepatier

1. Genotype 1 or 4 with **ONE** of the following:
    a. Treatment-naïve
        i. **Zepatier** – Genotype 1 and 4
            i. Patients with genotype 1a must have been tested for the NS5A resistance-associated polymorphisms
    b. Genotype 4: must be with Ribavirin (RBV)Treatment-experienced – previously treated with Peg-Interferon and Ribavirin (RBV)
        i. **Zepatier** – Genotype 1 and 4Patient's with genotype 1a must have been tested for the NS5A resistance-associated

polymorphisms

c. Treatment-experienced – previously treated with Protease Inhibitor (NS3)
    i. **Zepatier** – Genotype 1 only
        i. Patients with genotype 1a must have been tested for the NS5a resistance-associated polymorphisms.
        ii. Must be combined with Ribavirin (RBV)
d. **NO** Post-Transplant
e. End-Stage Renal disease (eGFR less than 30 ml/min/1.73m^2)
    i. **Zepatier** – Genotype 1 and 4

2. Genotype 3 with the following:
    a. **Zepatier** – Treatment-experienced – previously treated with Peg-Interferon and Ribavirin (RBV)
        i. Compensated cirrhosis – must be combined with Sovaldi

AND the following:
a. **NO** moderate or severe hepatic impairment (Child-Pugh Class B or C)

Vosevi

1. Genotype 1, 2, 3, 4, 5, or 6
    a. Treatment-experienced – previously treated with NS5A inhibitor
2. Genotype 1a, or 3
    a. Treatment Naïve
        i. Genotype 3 only
            1) Compensated cirrhosis - if Y93H mutation is present
    b. Treatment-experienced – previously treated with Peg-Interferon and Ribavirin
        i. Genotype 3 only
            1) No cirrhosis - if Y93H mutation is present
            2) Compensated cirrhosis
    c. Treatment-experienced
        i. Genotype 1a & 3
            1) Previously treated with Sovaldi without an NS5A inhibitor

AND ALL of the following:
a. Absence of severe renal impairment (eGFR less than 30 ml/min/1.73m^2) or end stage renal disease (ESRD) requiring hemodialysis

b. **NO** decompensated cirrhosis
c. **NO** moderate or severe hepatic impairment (Child-Pugh Class B or C)

Mavyret

1. Genotype 1, 2, 3, 4, 5, or 6
    a. Treatment-naïve
    b. Treatment-experienced – previously treated with Peg-Interferon and Ribavirin
    c. Treatment-experienced – previously treated with Sovaldi and Ribavirin (RBV)
    d. Post-transplant (liver and/or kidney transplant)

2. Genotype 1
    a. Treatment-experienced – previously treated with NS5A inhibitor without prior treatment with an NS3/4A protease inhibitor
    b. Treatment-experienced – previously treated with NS3/4A protease inhibitor without prior treatment with an NS5A inhibitor

3. Genotype 2
    a. Treatment experienced – Sovaldi with Ribavirin (RBV)

4. Unknown genotype
    a. Treatment-naïve

AND ALL of the following:
a. **NO** decompensated cirrhosis
b. **NO** moderate or severe hepatic impairment (Child-Pugh Class B or C)

AND ALL of the following for the Hepatitis C medications:
1. Presence of viral load (HCV RNA) in the serum prior to treatment
2. If the patient has a history of Hepatitis B (HBV) infection
    a. Prescriber agrees to monitor for HBV reactivation

Age 12 – 17 years of age

Diagnosis

Patient must have the following:

1. Chronic Hepatitis C
   a. Required documented viral load (HCV RNA) at least 6 months prior to request for treatment)

Harvoni

1. Genotype 1, 4, 5 or 6
   a. 35 kg or more
   b. **NO** decompensated cirrhosis

Sovaldi/Ribavirin (RBV)

1. Genotype 2 or 3
   a. 35 kg or more
   b. **NO** decompensated cirrhosis
   c. Must be combined with Ribavirin (RBV)

AND ALL of the following for the Hepatitis C medications:
1. Presence of viral load (HCV RNA) in the serum prior to treatment
2. If the patient has a history of Hepatitis B (HBV) infection
   a. Prescriber agrees to monitor for HBV reactivation

AND ALL of the following for the Hepatitis C medications if combined with ribavirin therapy:
1. Absence of significant or unstable cardiac disease
2. Neither the patient nor the partner of the patient is pregnant
3. If patient or their partner are of child bearing age, the patient has been or will be instructed to practice effective contraception during therapy and for 6 months after stopping ribavirin therapy

Prior – Approval *Renewal* Requirements

Harvoni only

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Chronic Hepatitis C – Genotype 1

a. Continuation of therapy for treatment-naïve patients , without cirrhosis, pre-treatment HCV RNA < 6 million IU/ml:
   i. Evaluation of patient at 4 weeks to determine that the viral load was not met within the 8 weeks of treatment

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration – 18 years of age and older

Genotype	Naïve / Experienced	No Cirrhosis	Compensated Cirrhosis	Decompensated Cirrhosis
1a	Naïve:	**Harvoni 8 weeks** (if RNA < 6M iU/ml) **Harvoni 12 weeks** (if RNA >= 6M iU/ml) **Epclusa 12 weeks** **Mavyret 8 weeks** Zepatier 12 weeks (if no NS5a RAS) Zepatier/RBV 16 weeks (if NS5a RAS present)	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier 12 weeks (if no NS5a RAS) Zepatier/RBV 16 weeks (if NS5a RAV present)	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV 12 weeks** **Epclusa 24 weeks**
1b		**Harvoni 8 weeks** (if RNA < 6M iU/ml) **Harvoni 12 weeks** (if RNA >= 6M iU/ml) **Epclusa 12 weeks** **Mavyret 8 weeks** Zepatier 12 weeks	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier 12 weeks	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV 12 weeks** **Epclusa 24 weeks**

1a	Experienced: Peg-INF and RBV	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 8 weeks** Zepatier 12 weeks (if no NS5a RAV) Zepatier/RBV 16 weeks (if NS5a RAV present)	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier 12 weeks (if no NS5a RAV) Zepatier/RBV 16 weeks (if NS5a RAV present)	**Harvoni/RBV** **12 weeks** **Harvoni 24 weeks** **Epclusa/RBV** **12 weeks** **Epclusa 24 weeks**
1b	Experienced: Peg-INF and RBV	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 8 weeks** Zepatier 12 weeks	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier 12 weeks	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV** **12 weeks** **Epclusa 24 weeks**
1	Experienced: Protease Inhibitor (NS3)	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier/RBV 12 weeks (Extend to 16wk if GT1a with NS5a RAS present)	**Harvoni/RBV 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier/RBV 12 weeks (Extend to 16wk if GT1a with NS5a RAS present)	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV** **12 weeks** **Epclusa 24 weeks**
1	Experienced: Sovaldi containing regimen that does NOT include NS5A	**Harvoni/RBV 12 weeks (for only SOF/RBV failure)** **Mavyret 12 weeks** (not previously treated with NS5A) **Vosevi 12 weeks** (for 1a only) **Epclusa 12 weeks** (for 1b only)	**Mavyret 12 weeks** **Vosevi 12 weeks** (for 1a only) **Epclusa 12 weeks** (for 1b only)	**Harvoni/RBV24 weeks** **Epclusa/RBV** **24 weeks**
1	Experienced: NS5A	**Vosevi 12 weeks** **Mavyret 16 weeks** (not previously treated with NS3/4)		**Harvoni/RBV** **24 weeks** **Epclusa/RBV** **24 weeks**
1	Post-Transplant Naïve:	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks**
1	Post-Transplant Experienced:	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks**

1	CKD stage 4 – 5/End-Stage Renal Disease	***Mavyret 8-16 weeks*** *(treatment determined by liver disease stage/prior treatments)* Zepatier 12 weeks	***Mavyret 8 - 16 weeks*** *(treatment determined by liver disease stage/prior treatments)* Zepatier 12 weeks	NONE
1	Hepatocellular Carcinoma	**Harvoni/RBV 12 weeks** **Epclusa/RBV 12 weeks**		
2	Naïve:	**Epclusa 12 weeks** **Mavyret 8 weeks**	**Epclusa 12 weeks** **Mavyret 12 weeks**	**Epclusa/RBV** **12 weeks** **Epclusa 24 weeks**
2	Experienced: Peg-INF and RBV	**Epclusa 12 weeks** **Mavyret 8 weeks**	**Epclusa 12 weeks** **Mavyret 12 weeks**	**Epclusa/RBV** **12 weeks** **Epclusa 24 weeks**
2	Experienced: NS5A	**Vosevi 12 weeks**		**Epclusa/RBV** **24 weeks**
2	Experienced: Sovaldi and RBV	**Epclusa 12 weeks** **Mavyret 12 weeks**	**Epclusa 12 weeks** **Mavyret 12 weeks**	**Epclusa/RBV** **24 weeks**
2	Post-Transplant Naïve:	**Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV** **12 weeks**
2	Post-Transplant Experienced:	**Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV** **12 weeks**
2	CKD stage 4 – 5/End-Stage Renal Disease	**Mavyret 8 – 16 weeks** *(treatment determined by liver disease stage/prior treatments)*	**Mavyret 8 – 16 weeks** *(treatment determined by liver disease stage/prior treatments)*	NONE
2	Hepatocellular Carcinoma	**Epclusa/RBV 12 weeks**		
3	Naïve:	**Epclusa 12 weeks** **Mavyret 8 weeks**	**Epclusa 12 weeks** (if Y93H mutation present, add RBV 12 weeks) **Mavyret 12 weeks** **Vosevi 12 weeks** (when Y93H present)	**Epclusa/RBV** **12 weeks** **Epclusa 24 weeks**

3	Experienced: Peg-INF and RBV	**Epclusa 12 weeks** (if Y93H mutation is present add RBV 12 weeks) **Mavyret 16 weeks** **Vosevi 12 weeks** (when Y93H mutation is present)	**Epclusa/ RBV 12 weeks** **Mavyret 16 weeks** Zepatier/Sovaldi 12 weeks **Vosevi 12 weeks**	**Epclusa/RBV 12 weeks** **Epclusa 24 weeks**
3	Experienced: Sovaldi and No Prior NS5A	**Mavyret 16 weeks** **Vosevi 12 weeks**		**Epclusa/RBV 24 weeks**
3	Experienced: NS5A	**Vosevi 12 weeks**	**Vosevi/RBV 12 weeks**	**Epclusa/RBV 24 weeks**
3	Post-Transplant Naïve:	**Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV 12 weeks**
3	Post-Transplant Experienced:	**Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Epclusa/RBV 12 weeks**
3	CKD stage 4 – 5/End-Stage Renal Disease	**Mavyret 8 – 16 weeks** (*treatment determined by liver disease stage/prior treatments)*	**Mavyret 8 – 16 weeks** (*treatment determined by liver disease stage/prior treatments)*	NONE
3	Hepatocellular Carcinoma	**Epclusa/RBV 12 weeks**		
4	Naïve:	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 8 weeks** Zepatier 12 weeks	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier 12 weeks	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV 12 weeks** **Epclusa 24 weeks**
4	Experienced: Peg-INF and RBV	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 8 weeks** Zepatier 12 weeks (if Relapsed after tx) Zepatier/RBV 16 weeks (if Failure on prior tx)	**Harvoni/RBV 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks** Zepatier 12 weeks (if Relapsed after tx) Zepatier/RBV 16 weeks (if Failure on prior tx)	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV 12 weeks** **Epclusa 24 weeks**
4	Experienced: NS5A	Vosevi 12 weeks		**Harvoni/RBV 24 weeks** Epclusa/RBV 24 weeks

4	Post-Transplant Naïve:	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks**
4	Post-Transplant Experienced:	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks**
4	CKD stage 4 – 5/End-Stage Renal Disease	Zepatier 12 weeks **Mavyret 8 - 16 weeks** *(treatment determined by liver disease stage/prior treatments)*		NONE
4	Hepatocellular Carcinoma	**Harvoni/RBV 12 weeks** **Epclusa/RBV 12 weeks**		
5 & 6	Naïve:	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 8 weeks**	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks**	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV 12 weeks** **Epclusa 24 weeks**
5 & 6	Experienced: Peg-INF and RBV	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 8 weeks**	**Harvoni 12 weeks** **Epclusa 12 weeks** **Mavyret 12 weeks**	**Harvoni/RBV 12 weeks** **Harvoni 24 weeks** **Epclusa/RBV 12 weeks** **Epclusa 24 weeks**
5 & 6	Experienced: NS5A	**Vosevi 12 weeks**		**Harvoni/RBV 24 weeks** **Epclusa/RBV 24 weeks**
5 & 6	Hepatocellular Carcinoma	**Harvoni/RBV 12 weeks** **Epclusa/RBV 12 weeks**		
5 & 6	CKD stage 4 – 5/End Stage Renal Disease	**Mavyret 8 - 16 weeks** *(treatment determined by liver disease stage/prior treatments)*	**Mavyret 8 - 16 weeks** *(treatment determined by liver disease stage/prior treatments)*	NONE
5 & 6	Post-Transplant	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks** **Mavyret 12 weeks** (liver and/or kidney transplant)	**Harvoni/RBV 12 weeks**
Unknown Genotype	Naïve	**Mavyret 8 weeks**	**Mavyret 12 weeks**	NONE

**** Bolded items are preferred products**

Duration – 12 to 17 years of age

Genotype	Naïve / Experienced	No Cirrhosis	Compensated Cirrhosis	Decompensated Cirrhosis
1	Naive	**Harvoni 12 weeks**	**Harvoni 12 weeks**	NONE
1	Experienced	**Harvoni 12 weeks**	**Harvoni 24 weeks**	NONE
4, 5 ,6	Naive/ Experienced	**Harvoni 12 weeks**	**Harvoni 12 weeks**	NONE
2	Naive/ Experienced	**Sovaldi/RBV 12 weeks**	**Sovaldi/RBV 12 weeks**	NONE
3	Naive/ Experienced	**Sovaldi/RBV 24 weeks**	**Sovaldi/RBV 24 weeks**	NONE

**** Bolded items are preferred products**

Harvoni	**8 weeks = (56 tablets per 56 days)**
Mavyret	**8 weeks = (168 tablets per 56 days)**
Mavyret	**12 weeks = (252 tablets per 84 days)**
Mavyret	**16 weeks = (336 tablets per 112 days)**
Zepatier	**12 weeks = (84 tablets per 84 days)**
Zepatier	**16 weeks = (112 tablets per 112 days)**

NS3/4a Protease Inhibitors:	NS5a Inhibitors	NS5B Polymerase Inhibitors
Telaprevir	Daclatasvir	Sofosbuvir (nuclear analog)
Boceprevir	Ledipasvir	Dasabuvir (non-nuclear analog)
Simeprevir	Ombitasvir	
Paritaprevir	Elbasvir	
Grazoprevir	Velpatasvir	
Voxilaprevir	Pibrentasvir	
Glecaprevir		

Prior – Approval *Renewal* Limits

Harvoni only

Treatment-Naïve, without cirrhosis, pre-treatment HCV RNA < 6 million IU/ml
4 weeks Harvoni (28 tablets per 28 days)

Rationale

Summary

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with hepatitis C virus (HCV) have no symptoms of the disease until liver damage becomes apparent, which may take several years. Safety and effectiveness of Epclusa, Mavyret, Vosevi and Zepatier in children less than 18 years of age have not been established. Safety and effectiveness of Harvoni and Sovaldi in children less than 12 years of age have not been established (2-8, 11).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Epclusa, Harvoni, Mavyret, Sovaldi, Vosevi, and Zepatier while maintaining optimal therapeutic outcomes.

References

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Policy History

Date	Action
December 2016	New addition to PA Merge of policy numbers 5.01.26, 5.01.32, 5.01.33, 5.01.36, 5.01.39, 5.01.40
March 2017	Annual editorial review Addition of – if Y93H mutation is present add RBV 12 weeks to Genotype 3 w/ no cirrhosis and to compensated cirrhosis treatment box Rewording of the Harvoni Genotype 1 only statement
April 2017	Addition of use of Harvoni and Sovaldi to criteria in patients age 12 – 17 who are at least 35 kg
June 2017	Annual review Addition of – treatment with Epclusa/RBV and Harvoni/RBV for patients with decompensated cirrhosis genotype 5 and 6 Additional requirement for Epclusa Genotype 3 "if Y93H mutation is present add RBV 12 weeks" for patients with no cirrhosis or compensated cirrhosis
August 2017	Addition of the following: hepatocellular carcinoma to Harvoni genotype 1, 4,5,6 and Epclusa genotype 1,2,3,4,5,6 and Daklinza genotype 1,2,3,4 ; Zepatier to genotype 3 and to end stage renal disease genotype 1 & 4; addition of Vosevi and Mavyret to new criteria Removal of Sovaldi /RBV from Hepatocellular carcinoma
September 2017	Annual review
October 2017	Updated all criteria to match AASLD HCV guidelines instituted on September 21st, 2017
December 2017	Annual editorial review Removal of the no history of alcohol and/or substance abuse in the past 6 months
April 2018	Annual editorial review Addition of Mavyret for genotype 1-6 that has treatment experience with Sovaldi and RBV Addition of unknown genotype in treatment naïve patients with and without compensated cirrhosis to Mavyret indications
August 2018	Addition of kidney and/or liver transplant to Mavyret criteria
November 2018	Annual review, Removal of Daklinza, Viekira, and Viekira XR

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on November 30, 2018 and is effective on January 1, 2019.