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Section:	Prescription Drugs	**Effective Date:**	July 1, 2023
Subsection:	Anti-Infective Agents	**Original Policy Date:**	December 9, 2016
Subject:	Hepatitis C Agents	**Page:**	1 of 19

Last Review Date: June 15, 2023

Hepatitis C Agents

Description

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

Preferred hepatitis C products: Epclusa, Harvoni, Mavyret, Sovaldi and Vosevi

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. **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 and pediatric patients 3 years of age and older with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infections (2):
    a. Without cirrhosis or with compensated cirrhosis
    b. With decompensated cirrhosis for use in combination with ribavirin

2. **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 virus (HCV) in adults and pediatric patients 3 years of age and older (3):
    a. Genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
    b. Genotype 1 infection with decompensated cirrhosis, in combination with ribavirin
    c. Genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin

3. **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 and pediatric patients 3 years and older 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 and pediatric patients 3 years and older 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 (4).

4. **Sovaldi** is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of (5):
    a. Adult patients with genotype 1, 2, 3 or 4 chronic hepatitis C infection without cirrhosis or with compensated cirrhosis as a component of a combination antiviral treatment regimen
    b. Pediatric patients 3 years of age and older with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin

5. **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 (6):
    a. Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
    b. Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor

i. 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

6. **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 for treatment of chronic HCV genotype 1 or 4 infection in adult and pediatric patients 12 years of age and older or weighing at least 30 kg. Zepatier is indicated for use with ribavirin in certain patient populations (7).

7. **Ribavirin** is a nucleoside analogue indicated in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age or older with compensated liver disease (8).

No dose adjustment in direct-acting antivirals (DAAs) dosing is required in patients with renal impairment when using the recommended regimens (2-8).

Mavyret and Zepatier are contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C) due to potential toxicity. Mavyret is also contraindicated in patients with any history of prior hepatic decompensation (4,7).

Ribavirin has boxed warnings regarding embryo-fetal toxicity, hemolytic anemia, and monotherapy not recommended. Ribavirin therapy is contraindicated in women who are pregnant and in men whose female partners 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 (8).

If a 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 (8).

Epclusa, Harvoni, Mavyret, Sovaldi, Vosevi and Zepatier have a 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 (2-7).

The safety and effectiveness of Vosevi in pediatric patients less than 18 years of age have not been established (6).

The safety and effectiveness of Zepatier in pediatric patients less than 12 years old or weighing less than 30 kg have not been established (7).

The safety and effectiveness of Epclusa, Harvoni, Mavyret, and Sovaldi in pediatric patients less than 3 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, Harvoni, Mavyret, Sovaldi, Vosevi and Zepatier may be considered **medically necessary** if the conditions indicated below are met.

Epclusa, Harvoni, Mavyret, Sovaldi, Vosevi and Zepatier may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

1. Hepatitis C

   AND ONE of the following:
   a. Required documented viral load (HCV RNA) at least 6 months prior to request for treatment
   b. Patient has a poor prognosis and treatment cannot be delayed
   c. Past history of hepatitis C infection is evident or suspected

AND ALL of the following:

a. Presence of viral load (HCV RNA) in the serum prior to treatment
b. If the patient has a history of hepatitis B (HBV) infection
   i. Prescriber agrees to monitor for HBV reactivation

AND the following for each listed medication**:**

Epclusa

1. 3 years of age and older
2. Genotype 1, 2, 3, 4, 5, or 6

AND ONE of the following:

1. Treatment naïve
   a. With or without cirrhosis
      i. If decompensated cirrhosis must be used in combination with ribavirin, unless ribavirin ineligible
2. Treatment experienced with peginterferon alfa/ribavirin with or without an HCV NS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir)
   a. With or without cirrhosis
      i. If decompensated cirrhosis must be used in combination with ribavirin, unless ribavirin ineligible
3. Treatment experienced with sofosbuvir or an NS5A inhibitor [(9)] (see Appendix 1)
   a. Decompensated cirrhosis
4. Post liver transplant [(10)]
   a. Treatment naïve or treatment experienced
   b. With or without cirrhosis
      i. If decompensated cirrhosis must be used in combination with ribavirin
5. Post kidney transplant [(11)]
   a. **NO** decompensated cirrhosis

AND ALL of the following **if combined with ribavirin therapy**:

1. **NO** significant or unstable cardiac disease
2. Females of reproductive potential **only**: pregnancy will be excluded before start of treatment, and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose
3. Males with female partners of reproductive potential **only**: pregnancy will be excluded before start of treatment and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

Harvoni

1. 3 years of age and older

AND ONE of the following:

1. Genotype 1 with **ONE** of the following:
    a. Treatment naïve **without** cirrhosis
        i. If pretreatment HCV RNA is less than 6 million IU/mL, prescriber must agree to draw week 4 HCV RNA level
    b. Treatment naïve **with** cirrhosis
        i. Compensated or decompensated cirrhosis
        ii. If decompensated cirrhosis, must be used in combination with ribavirin
    c. Treatment experienced with peginterferon +/- ribavirin with or without an NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir)
        i. With or without cirrhosis
        ii. If decompensated cirrhosis, must be used in combination with ribavirin
2. Genotype 4, 5 or 6 :
    a. Treatment naïve or treatment experienced with peginterferon +/- ribavirin with or without an NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir)
    b. **NO** decompensated cirrhosis
3. Post liver transplant [10]
    a. Genotype 1, 4, 5 or 6
    b. Treatment naïve or experienced
    c. With or without cirrhosis
        i. If decompensated cirrhosis must be used in combination with ribavirin
4. Post kidney transplant [11]
    a. Genotype 1, 4, 5 or 6
    b. Treatment naïve or experienced
    c. **NO** decompensated cirrhosis

AND ALL of the following **if combined with ribavirin therapy**:

1. **NO** significant or unstable cardiac disease
2. Females of reproductive potential **only**: pregnancy will be excluded before start of treatment, and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

3. Males with female partners of reproductive potential **only**: pregnancy will be excluded before start of treatment and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

Mavyret

1. 3 years of age and older
2. **NO** moderate or severe hepatic impairment (Child-Pugh Class B or C)
3. **NO** decompensated cirrhosis

AND ONE of the following:

1. Treatment naïve
    a. Genotype 1, 2, 3, 4, 5, 6 or unknown
2. Treatment experienced and **ONE** of the following:
    a. Previously treated with peginterferon, ribavirin and an NS5A inhibitor, without prior treatment with an NS3/4A protease inhibitor (see Appendix 1)
        i. Genotype 1
    b. Previously treated with peginterferon, ribavirin and an NS3/4A protease inhibitor, without prior treatment with an NS5A inhibitor (see Appendix 1)
        i. Genotype 1
    c. Previously treated with peginterferon and ribavirin with or without sofosbuvir, without prior treatment with an NS3/4A protease inhibitor or NS5A inhibitor (see Appendix 1)
        i. Genotype 1, 2, 3, 4, 5 or 6
3. Post kidney/liver transplant
    a. Genotype 1, 2, 3, 4, 5 or 6

Sovaldi

AND ONE of the following:

1. Genotype 1 or 4
    a. 18 years of age and older
    b. Treatment naïve
    c. **NO** decompensated cirrhosis
    d. Used in combination with peginterferon and ribavirin
        i. **Genotype 1**: Sovaldi can be used alone if ineligible for interferon-based

regimen

2. Genotype 2 or 3
    a. 3 years of age and older
    b. Treatment naive or treatment experienced with peginterferon +/- ribavirin
    c. **NO** decompensated cirrhosis
    d. Used in combination with ribavirin
3. Hepatocellular carcinoma
    a. 18 years of age and older
    b. Genotype 1, 2, 3 or 4
    c. Awaiting liver transplantation
    d. Used in combination with ribavirin

AND ALL of the following **if combined with ribavirin therapy**:

1. **NO** significant or unstable cardiac disease
2. Females of reproductive potential **only**: pregnancy will be excluded before start of treatment, and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose
3. Males with female partners of reproductive potential **only**: pregnancy will be excluded before start of treatment and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

Vosevi

1. 18 years of age and older
2. Genotype 1, 2, 3, 4, 5 or 6
3. **NO** decompensated cirrhosis

AND ONE of the following:

1. Treatment experienced with **ONE** of the following:
    a. Previously treated with an NS5A inhibitor (see Appendix 1)
    b. Previously treated with a sofosbuvir-based regimen[9]
        i. **Genotype 3:** if compensated cirrhosis, must be used in combination with ribavirin unless ribavirin ineligible
2. Post liver/kidney transplant [10,11]
    a. Previously treated with a Direct Acting Antiviral (DAA) (see Appendix 1)

AND ALL of the following **if combined with ribavirin therapy**:

1. **NO** significant or unstable cardiac disease

2. Females of reproductive potential **only**: pregnancy will be excluded before start of treatment, and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose
3. Males with female partners of reproductive potential **only**: pregnancy will be excluded before start of treatment and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

Zepatier

1. 12 years of age and older **OR** weighing at least 30 kg
2. **NO** moderate or severe hepatic impairment (Child-Pugh Class B or C)
3. **NO** liver transplant or waiting for a liver transplant
4. **NO** decompensated cirrhosis
5. Patient **MUST** have a contraindication to at least **TWO** of the preferred products (Epclusa, Harvoni, Mavyret, Sovaldi and Vosevi)

AND ONE of the following:

1. Treatment naïve:
   a. Genotype 1a, 1b or 4
      i. **Genotype 1a**: must be tested for NS5A resistance-associated polymorphisms. If positive, must be used in combination with ribavirin
2. Treatment experienced with peginterferon and ribavirin
   a. Genotype 1a, 1b or 4
      i. **Genotype 1a**: must be tested for NS5A resistance-associated polymorphisms. If positive, must be used in combination with ribavirin
      ii. **Genotype 4**: must be used in combination with ribavirin
3. Treatment experienced with peginterferon, ribavirin and an NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir)
   a. Genotype 1a or 1b
   b. Must be used in combination with ribavirin

AND ALL of the following **if combined with ribavirin therapy**:

1. **NO** significant or unstable cardiac disease
2. Females of reproductive potential **only**: pregnancy will be excluded before start of treatment, and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

3. Males with female partners of reproductive potential **only**: pregnancy will be excluded before start of treatment and patient will be advised to use effective contraception during treatment with ribavirin and for 6 months after the final dose

Prior – Approval *Renewal* Requirements

Harvoni Only

Age 3 years of age and older

Diagnosis

Patient must have the following:

1. Hepatitis C
    a. Genotype 1
    b. 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 has been performed

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

EPCLUSA Treatment Duration		
HCV Genotype	**Patient Population**	**Treatment Regimen and Duration**
1, 2, 3, 4, 5, 6	Treatment naïve **or** Treatment experienced with **Peg-INF/RBV** +/- **NS3/4A PI** **NO** decompensated cirrhosis	Epclusa 12 weeks
	Treatment naïve **or** Treatment experienced with **Peg-INF/RBV** +/- **NS3/4A PI** **Decompensated** cirrhosis	Epclusa + RBV 12 weeks **or** Epclusa 24 weeks, ***if RBV ineligible***[12]
	Treatment experienced with **sofosbuvir** or **NS5A inhibitor** [9] **Decompensated** cirrhosis	Epclusa + RBV 24 weeks
	Post kidney[11] transplant	Epclusa 12 weeks

	NO decompensated cirrhosis	
	Post liver [10] transplant **NO** decompensated cirrhosis	Epclusa 12 weeks
	Post liver[10] transplant Treatment naïve **Decompensated** cirrhosis	Epclusa + RBV 12 weeks
	Post liver[10] transplant Treatment experienced **Decompensated** cirrhosis	Epclusa + RBV 24 weeks

EPCLUSA Dosing		
Age/Weight	**EPCLUSA Strength**	**Quantity per day**
Age 18+	400 mg/100 mg tablet	1/day
Age 3-17 and weight 30kg or greater	400 mg/100 mg tablet **or** 200 mg/50 mg tablet 200 mg/50 mg packet of pellets	1/day **or** 2/day **or** 2/day
Age 3-17 and weight 17kg to < 30kg	200 mg/50 mg tablet **or** 200 mg/50 mg packet of pellets	1/day **or** 1/day
Age 3-17 and weight <17kg	150 mg/37.5 mg packet of pellets	1/day

HARVONI Treatment Duration		
HCV Genotype	**Patient Population**	**Treatment Regimen and Duration**
1	Treatment naïve **NO** cirrhosis *Pretreatment HCV RNA < than 6 million IU/ML*	Harvoni 8 weeks, ***Must repeat viral load testing at week 4***
	Treatment naïve **NO** cirrhosis *Pretreatment HCV RNA > than 6 million IU/ML*	Harvoni 12 weeks
	Treatment naïve **Compensated** cirrhosis	Harvoni 12 weeks
	Treatment naïve **or** Treatment experienced with **Peg-INF** +/- **RBV** and +/- **NS3/4A PI** **Decompensated** cirrhosis	Harvoni + RBV 12 weeks
	Treatment experienced with **Peg-INF** +/- **RBV** and +/- **NS3/4A PI** **NO** cirrhosis	Harvoni 12 weeks
	Treatment experienced with **Peg-INF** +/- **RBV** and +/- **NS3/4A PI** **Compensated** cirrhosis	Harvoni 24 weeks **or** Harvoni + RBV 12 weeks ***if RBV eligible***
4, 5, 6	Treatment naïve **or** Treatment experienced with **Peg-INF** +/- **RBV** and +/- **NS3/4A PI** **NO** decompensated cirrhosis	Harvoni 12 weeks
1, 4, 5, 6 *Liver transplant* [10]	Treatment naïve/experienced Liver transplant **NO** decompensated cirrhosis	Harvoni 12 weeks

	Treatment naïve Liver transplant **Decompensated** cirrhosis	Harvoni + RBV 12 weeks
	Treatment experienced Liver transplant **Decompensated** cirrhosis	Harvoni + RBV 24 weeks
1, 4, 5, 6 *Kidney transplant* (11)	Treatment naïve/experienced Kidney transplant **NO** decompensated cirrhosis	Harvoni 12 weeks

HARVONI Dosing		
Age/Weight	**Strength**	**Quantity per day**
18 years old +	90/400 mg tablet	1/day
Age 3-17 and weight 35kg or greater	90/400 mg tablet **or** 45/200 mg packet of pellets	1/day **or** 2/day
Age 3-17 and weight 17kg to <35kg	45/200 mg packet of pellets	1/day
Age 3-17 and <17kg	33.75/150 mg packet of pellets	1/day

MAVYRET Treatment Duration		
HCV Genotype	**Patient Population**	**Treatment Regimen and Duration**
1, 2, 3, 4, 5, 6 or unknown	Treatment naïve **NO** decompensated cirrhosis	Mavyret 8 weeks
1**	Treatment experienced with **Peg-INF/RBV + NS5A inhibitor** **NO** prior treatment with an **NS3/4A PI** **NO** decompensated cirrhosis	Mavyret 16 weeks**
1	Treatment experienced with **Peg-INF/RBV + NS3/4A PI** **NO** prior treatment with an **NS5A inhibitor** **NO** decompensated cirrhosis	Mavyret 12 weeks
1, 2, 4, 5, 6	Treatment experienced with **Peg-INF/RBV** +/- **sofosbuvir** **NO** prior treatment with **NS3/4A PI** or **NS5A inhibitor** **NO** cirrhosis	Mavyret 8 weeks
	Treatment experienced with **Peg-INF/RBV** +/- **sofosbuvir** **NO** prior treatment with **NS3/4A PI** or **NS5A inhibitor** **Compensated** cirrhosis	Mavyret 12 weeks
3**	Treatment experienced with **Peg-INF/RBV** +/- **sofosbuvir** **NO** prior treatment with **NS3/4A PI or NS5A inhibitor** **NO** decompensated cirrhosis	Mavyret 16 weeks**
1, 2, 3, 4, 5, 6 Liver / Kidney Transplant	Liver / kidney transplant recipients **NO** decompensated cirrhosis	Mavyret 12 weeks **or** Mavyret 16 weeks, ***if genotype 1 or 3 treatment experienced*****

** ***Genotype 1*** *(NS5A inhibitor experienced without prior treatment with an NS3/4A protease inhibitor)*

		****Genotype 3*** (Peg-INF/RBV +/- sofosbuvir experienced, without prior treatment with NS3/4A PI or NS5A inhibitor)

MAVYRET Dosing		
Age/Weight	**Strength**	**Quantity per Day**
Age 12+	100 mg/40 mg tablet	3/day
Age 3-11 and weight 45kg or greater***	100 mg/40 mg tablet or 50 mg/20 mg packet of pellets	3/day **or** 6/day
Age 3-11 and weight 30kg to <45kg	50 mg/20 mg packet of pellets	5/day
Age 3-11 and weight 20kg to <30kg	50 mg/20 mg packet of pellets	4/day
Age 3-11 and <20kg	50 mg/20 mg packet of pellets	3/day
***Pediatric patients weighing 45 kg and greater who are unable to swallow tablets may take **six** 50 mg/20 mg packets of oral pellets once daily. Dosing with oral pellets has not been studied for pediatric patients weighing greater than 45 kg.		

SOVALDI Treatment Duration		
HCV Genotype	**Patient Population**	**Treatment Regimen and Duration**
1 Age 18+ only	Treatment naïve	Sovaldi + Peg-INF + RBV 12 weeks **or** Sovaldi + RBV 24 weeks, ***if interferon ineligible***
2 Age 3+	Treatment naïve **or** Treatment experienced with **Peg-INF +/- RBV**	Sovaldi + RBV 12 weeks
3 Age 3+	Treatment naïve **or** Treatment experienced with **Peg-INF +/- RBV**	Sovaldi + RBV 24 weeks
4 Age 18+ only	Treatment naïve	Sovaldi + Peg-INF + RBV 12 weeks
1, 2, 3, 4 Age 18+ only	Hepatocellular carcinoma Awaiting liver transplantation	Sovaldi + RBV up to 48 weeks

SOVALDI Dosing		
Age/Weight	**Strength**	**Quantity per Day**
Age 18+	400 mg tablet	1/day
Age 3-17 and weight at least 35 kg	400 mg tablet **or** 200 mg tablet **or** 200 mg pellets	1/day **or** 2/day **or** 2/day
Age 3-17 and weight 17 to <35kg	200 mg tablet **or** 200 mg pellets	1/day **or** 1/day
Age 3-17 and weight <17 kg	150 mg pellets	1/day

VOSEVI Treatment Duration

HCV Genotype	Patient Population	Treatment Regimen and Duration
1, 2, 3, 4, 5, 6	Treatment experienced with an **NS5A inhibitor** **NO** decompensated cirrhosis	Vosevi 12 weeks
1, 2, 3, 4, 5, 6 (9)	Treatment experienced with **sofosbuvir** **NO** decompensated cirrhosis	Vosevi 12 weeks
3 (9)	Treatment experienced with **sofosbuvir** **Compensated** cirrhosis	Vosevi 12 weeks + RBV, ***If RBV eligible***
1, 2, 3, 4, 5, 6 Liver / Kidney transplant (10,11)	Treatment experienced with a **DAA** Liver / kidney transplant **NO** decompensated cirrhosis	Vosevi 12 weeks +/- RBV

VOSEVI Dosing	
Strength	**Quantity per day**
400 mg/100 mg/100 mg tablet	1/day

ZEPATIER Treatment Duration		
HCV Genotype	**Patient Population**	**Treatment Regimen and Duration**
1**a**	Treatment naïve **NEGATIVE** for NS5A polymorphism	Zepatier 12 weeks
	Treatment naïve **POSITIVE** for NS5A polymorphism	Zepatier + RBV 16 weeks
	Treatment experienced with **Peg-INF/RBV** **NO** decompensated cirrhosis **NEGATIVE** for NS5A polymorphism	Zepatier 12 weeks
	Treatment experienced with **Peg-INF/RBV** **POSITIVE** for NS5A polymorphism	Zepatier + RBV 16 weeks
	Treatment experienced with **Peg-INF/RBV + NS3/4A PI** The optimal Zepatier based treatment regimen and duration of therapy for Peg-INF/RBV + NS3/4A PI experienced, genotype 1a, positive for NS5A polymorphism has not been established. NS5A polymorphism testing is not needed for this patient population.	Zepatier + RBV 12 weeks
1**b**	Treatment naïve	Zepatier 12 weeks
	Treatment experienced with **Peg-INF/RBV**	Zepatier 12 weeks
	Treatment experienced with **Peg-INF/RBV + NS3/4A PI**	Zepatier + RBV 12 weeks
4	Treatment naïve	Zepatier 12 weeks
	Treatment experienced with **Peg-INF/RBV**	Zepatier + RBV 16 weeks

ZEPATIER Dosing	
Strength	**Quantity per day**
50 mg/100 mg tablet	1/day

Prior – Approval *Renewal* Limits

Harvoni Only

HARVONI Treatment Duration		
HCV Genotype	**Patient Population**	**Treatment Regimen and Duration**
1	Treatment naïve **NO** cirrhosis Pretreatment HCV RNA < 6 million IU/ML	Harvoni 4 weeks **(1 renewal only)**

HARVONI Dosing		
Age/Weight	**Strength**	**Quantity per Day**
Age 18+	90/400 mg tablet	1/day
Age 3-17 and weight 35kg or greater	90/400 mg tablet 45/200 mg packet of pellets	1/day **or** 2/day
Age 3-17 and weight 17kg to <35kg	45/200 mg packet of pellets	1/day
Age 3-17 and weight <17kg	33.75/150 mg packet of pellets	1/day

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 Vosevi in pediatric patients less than 18 years of age have not been established. The safety and effectiveness of Zepatier in patients less than 12 years of age or weighing less than 30kg have not been established. The safety and effectiveness of Epclusa, Harvoni, Mavyret and Sovaldi in pediatric patients less than 3 years of age have not been established (1-8).

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 Viekira, and Viekira XR
May 2019	Changed age requirement for Mavyret from 18 and older to 12 and older or patient weighs ≥ 45 kg
June 2019	Annual review. Revised Mavyret treatment durations chart to include no prior NS3/4 or NS5A for certain genotypes
July 2019	Removed Daklinza from policy due to being discontinued
September 2019	Annual review and reference update. Changed Harvoni and Sovaldi age limits to 3 and older and removed weight requirement. Added Harvoni/RBV to Genotype 1 for decompensated cirrhosis and Genotype 1 and 4 for post-transplant, no decompensated cirrhosis
October 2019	Revised Mavyret treatment naïve patients, all genotypes and unknown genotype with compensated cirrhosis to 8 week durations
December 2019	Annual review. Addition of requirement to have a contraindication to preferred products. Added Epclusa to chart for CKD for all genotypes for adults with no cirrhosis or compensated cirrhosis. Removed requirement for no renal impairment for Harvoni, Epclusa, and Vosevi
April 2020	Removed "chronic" from the required diagnosis and added patient has a poor prognosis and treatment cannot be delayed or past Hep C infection is evident or suspected per SME. Revised age limit for Epclusa to 6 years of age or older or weight 17kg or greater
June 2020	Annual review. Added Harvoni 33.75/150 mg and Sovaldi 150 mg for pediatric patients less than 17kg
August 2020	Revised chart for all genotypes for post-transplant patients (Harvoni and Epclusa)
September 2020	Annual review
June 2021	Annual review and reference update

July 2021	Epclusa and Mavyret age reduced to 3 and older and no longer has a minimum weight requirement. Added new Mavyret and Epclusa dosage form: packets of pellets. Revised all sections to align with the most up to date AASLD/IDSA HCV guidelines and package inserts.
September 2021	Annual review
January 2022	Per package insert update: Zepatier age reduced to 12 years and older or weighing at least 30 kg
March 2022	Annual review and reference update
June 2023	Annual editorial review. Clarified that Harvoni can have only 1 renewal of 4 weeks. Changed policy number to 5.01.041

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 15, 2023 and is effective on July 1, 2023.

Appendix 1

Direct Acting Antivirals (DAAs)		
NS3/4A Protease Inhibitors	**NS5A Inhibitors**	**NS5B Polymerase Inhibitors**
boceprevir (Victrelis)	daclatasvir (Daklinsa)	dasabuvir non-nuclear analog *(component of Viekira Pak)*
glecaprevir *(component of Mavyret)*	elbasvir *(component of Zepatier)*	sofosbuvir (Sovaldi) nuclear analog *(component of Epclusa, Harvoni, Vosevi)*
grazoprevir *(component of Zepatier)*	ledipasvir *(component of Harvoni)*	
paritaprevir *(component of Viekira Pak and Technivie)*	ombitasvir *(component of Viekira Pak and Technivie)*	
simeprevir (Olysio)	pibrentasvir (component of Mavyret)	
telaprevir (Incivek)	velpatasvir *(component of Epclusa and Vosevi)*	
voxilaprevir *(component of Vosevi)*		