MEDICATION POLICY

Generic Name: Ledipasvir/Sofosbuvir

Therapeutic Class or Brand Name: Harvoni®

Applicable Drugs (if Therapeutic Class)**:** N/A

Date of Origin: 10/24/14 **Date Last Reviewed/Revised:** 5/18/2018

GPI Code: 1235990240

Prior Authorization Criteria (may be considered medically necessary when criteria I through VII are met):

I. Documented diagnosis of chronic hepatitis C (CHC) genotypes 1, 4, 5, or 6 infection.

II. Documentation that patient meets ONE of the following criteria A, B, or C:

- A. Has a Metavir score of F3 (advanced fibrosis) or F4 (compensated cirrhosis).
- B. Is post-liver transplant.
- C. Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2:
  1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis).
  2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis.

III. Documentation of patient's Hepatitis C treatment history and baseline viral load.

IV. Documentation that patient meets ONE of the following criteria A through C:

- A. Patient has genotype 1 AND meets ONE of criteria 1 through 4:
  1. Patient meets ALL of criteria a through c below:
     - a. Patient has a documented contraindication to Mavyret™ and Zepatier™.
     - b. Patient meets ONE of criteria i or ii:
       - i Patient has a documented contraindication to Epclusa® and Vosevi®.
       - ii Patient is treatment-naïve, without cirrhosis, non-black, HIV-uninfected, and has a pre-treatment HCV RNA < 6 million IU/ml.
     - c. Patient meets ONE of criteria i, ii, or iii:
       - i Patient does not have cirrhosis.
       - ii Patient has compensated cirrhosis, but has not failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir or boceprevir).

iii If patient has compensated cirrhosis, and has failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir or boceprevir), then patient must also meet ONE of criteria aa or bb:

aa. Harvoni® is prescribed in combination with ribavirin.

bb. Patient has a documented intolerance or contraindication to ribavirin.

2. Patient has decompensated cirrhosis (Child-Pugh B or C) AND meets BOTH of criteria a and b:
   a. Patient has a documented contraindication to Epclusa®.
   b. Patient meets ONE of criteria i or ii:
      i Harvoni® is prescribed in combination with ribavirin.
      ii Patient has a documented intolerance or contraindication to ribavirin.
3. Patient is post-liver transplant and criterion a is met:
   a. Patient has a documented contraindication to Mavyret™.
4. Patient has failed prior treatment with a non-NS5A inhibitor, sofosbuvir-containing regimen and criterion a is met:
   a. Patient has a documented contraindication to Mavyret™.

B. Patient has genotype 4 AND meets ONE of criteria 1 through 3:

1. Patient meets BOTH of criteria a and b below:
   a. Patient has a documented contraindication to Mavyret™, Zepatier™, and Epclusa®.
   b. Patient meets ONE of criteria i, ii, or iii:
      i Patient does not have cirrhosis.
      ii Patient has compensated cirrhosis, but has not failed prior treatment with peginterferon + ribavirin.
      iii If patient has compensated cirrhosis, and has failed prior treatment with peginterferon + ribavirin, then patient must also meet ONE of criteria aa or bb:

aa. Harvoni® is prescribed in combination with ribavirin.

bb. Patient has a documented intolerance or contraindication to ribavirin.

2. Patient has decompensated cirrhosis (Child-Pugh B or C) AND meets BOTH of criteria a and b:
   a. Patient has a documented contraindication to Epclusa®.
   b. Patient meets ONE of criteria i or ii:
      i Harvoni® is prescribed in combination with ribavirin.

ii Patient has a documented intolerance or contraindication to ribavirin.

3. Patient is post-liver transplant and criterion a is met:

a. Patient has a documented contraindication to Mavyret™.

C. Patient has genotypes 5 or 6 and criterion 1 is met:

1. Patient has a documented contraindication to Mavyret™ and Epclusa®.

V. Documentation that patient's hepatitis C drug therapy is prescribed as outlined in the table under Authorization in the Approval Length section.

VI. Minimum age requirement: 12 years old.

VII. Prescriber is a Gastroenterologist, Infectious Disease Specialist, or Hepatologist.

Exclusion Criteria:

- As retreatment when there has been relapse after, or no response to, a prior treatment course with Daklinza™ (daclatasvir), Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/sofosbuvir), Mavyret™ (glecaprevir/pibrentasvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir), Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir), or Zepatier™ (elbasvir/grazoprevir).
- Coadministration of Harvoni® with P-gp inducers or any of the drugs listed in the table below:

Drug Class	Drugs within class
Antiarrhythmics	Amiodarone
Anticonvulsants	Carbamazepine, phenytoin, phenobarbital, oxcarbazepine
Antimycobacterials	Rifabutin, rifampin, rifapentine
Herbal Supplements	St. John's wort (*Hypericum perforatum*)
HIV Antiretrovirals	Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir), tipranavir/ritonavir
HMG-CoA Reductase Inhibitors	Rosuvastatin
NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection	Daklinza™ (daclatasvir), Epclusa® (sofosbuvir/velpatasvir), Mavyret™ (glecaprevir/pibrentasvir), Olysio® (simeprevir), Sovaldi® (sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Victrelis® (boceprevir), Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir), Vosevi® (sofosbuvir/velpatasvir/voxilaprevir), Zepatier™ (elbasvir/grazoprevir)

Other Criteria:

- N/A

Quantity/Days Supply Restrictions:

- 28 tablets per 28 days.

Approval Length:

- **Authorization:** See table directly below.

Drug Therapy	Cirrhosis	G1a		G1b		G4		G5		G6	
		TN	TE	TN	TE	TN	TE	TN	TE	TN	TE
Harvoni®	No	12w	12w[5]	12w	12w[5]	12w	12w[1]	12w	12w[1]	12w	12w[1]
	No & low HCV RNA[*]	8w[*]		8w[*]							
	Comp	12w	24w[5]	12w	24w[5]	12w	12w[1]	12w	12w[1]	12w	12w[1]
	Decomp	24w		24w		24w		24w		24w	
Harvoni® + RBV	No		12w[9x]		12w[9x]						
	No & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]
	Comp		12w[5]		12w[5]		12w[1]				
	Comp & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]
	Decomp	12w	24w[11]	12w	24w[11]	12w	24w[11]	12w	24w[11]	12w	24w[11]
	Decomp & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w^	12w^	12w^	12w[^]

TN = treatment naïve; TE = treatment experienced; Comp = compensated; Decomp = decompensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks
[x]Except in patients who have failed simeprevir.
[*]Harvoni® for 8 weeks may be considered in G1 treatment-naïve patients without cirrhosis who are non-black, HIV-uninfected, and have a pre-treatment HCV RNA < 6 million IU/ml.
[^]For patients who develop HCV infection post-liver transplantation.
[1]For patients who have failed pegIFN/RBV.
[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.
[9]For patients who have failed a non-NS5A inhibitor, sofosbuvir-containing regimen.
[11]For patients who failed a sofosbuvir-based treatment only.

- **Re-Authorization:** N/A

Appendix:

N/A

Disclaimer: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgment in providing the most appropriate care for their patients.

MEDICATION POLICY

References:

1. http://hcvguidelines.org/full-report-view.
2. http://www.bcbsnc.com/assets/services/public/pdfs/formulary/Harvoni_UM_Criteria.pdf.
3. http://blue.regence.com/trgmedpol/drugs/dru366.pdf.
4. Medi-Span.
5. http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf.
6. http://www.fda.gov/Drugs/DrugSafety/ucm439484.htm.

MEDICATION POLICY

Historical Tracking Of Changes Made To Policy	
5/18/2018	**1. No change**
10/30/2017	2. **Changed** "IV. A. 1. a. Patient has a documented contraindication to Zepatier™" **to** "IV. A. 1. a. Patient has a documented contraindication to Mavyret™ and Zepatier™" **under Prior Authorization Criteria**. 3. **Changed** "IV. A. 1. b. i. Patient has a documented contraindication to Epclusa®" **to** "IV. A. 1. b. i. Patient has a documented contraindication to Epclusa® and Vosevi®" **under Prior Authorization Criteria**. 4. **Changed** "IV. A. 1. c. ii. Patient has compensated cirrhosis, but has not failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir)" **to** "IV. A. 1. c. ii. Patient has compensated cirrhosis, but has not failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir, or boceprevir)" **under Prior Authorization Criteria**. 5. **Changed** "IV. A. 1. c. iii. If patient has compensated cirrhosis, and has failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir)…" **to** "IV. A. 1. c. iii. If patient has compensated cirrhosis, and has failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir or boceprevir)…" **under Prior Authorization Criteria**. 6. **Changed** "IV. A. b. ii. Patient is treatment-naïve without cirrhosis and has a pre-treatment HCV RNA < 6 million IU/ml)" **to** "IV. A. b. ii. Patient is treatment-naïve, without cirrhosis, non-black, HIV-uninfected, and has a pre-treatment HCV RNA < 6 million IU/ml" **under Prior Authorization Criteria**. 7. **Changed** "IV. A. 2. Patient has decompensated cirrhosis (Child-Pugh B)…" **to** "IV. A. 2. Patient has decompensated cirrhosis (Child-Pugh B or C)…" **under Prior Authorization Criteria**. 8. **Changed** "IV. A. 3. Patient is post-liver transplant and meets ONE of criteria a or b: a. Harvoni® is prescribed in combination with ribavirin; b. Patient has a documented intolerance or contraindication to ribavirin" **to** "IV. A. 3. Patient is post-liver transplant and criterion a is met: a. Patient has a documented contraindication to Mavyret™" **under Prior Authorization Criteria**. 9. **Changed** "IV. A. 4. Patient has failed prior treatment with Sovaldi® + ribavirin +/- peginterferon" **to** "IV. A. 4. Patient has failed prior treatment with a non-NS5A inhibitor, sofosbuvir-containing regimen and criterion a is met: a. Patient has a documented contraindication to Mavyret™" **under Prior Authorization Criteria**. 10. **Changed** "B. 1. A. Patient has a documented contraindication to Zepatier™ and Epclusa®" **to** "B. 1. A. Patient has a documented contraindication to Mavyret™, Zepatier™, and Epclusa®" **under Prior Authorization Criteria**. 11. **Changed** "IV. B. 2. Patient has decompensated cirrhosis (Child-Pugh B)…"**to** "IV. B. 2. Patient has decompensated cirrhosis (Child-Pugh B or C)…" **under Prior Authorization Criteria**. 12. **Changed** "Patient is post-liver transplant and meets ONE of criteria a or b: a. Harvoni® is prescribed in combination with ribavirin; b. Patient has a documented intolerance or contraindication to ribavirin" **to** "IV. B. 3. Patient is post-liver transplant and criterion a is met: a. Patient has a documented contraindication to Mavyret™" **under Prior Authorization Criteria**. 13. **Changed** "IV. C. 1. Patient has a documented contraindication to Epclusa®" **to** "" **under Prior Authorization Criteria**. 14. **Changed** "VI. Minimum age requirement: 18 years old" **to** "Minimum age requirement: 12 years old" **under Prior Authorization Criteria**. 15. **Removed** "Child-Pugh C" **from Exclusion Criteria**. 16. **Added** "Mavyret™ (glecaprevir/pibrentasvir)" **and** "Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)" **to** list of drugs following the statement "As retreatment when there has been relapse after, or no response to, a prior treatment course with…" **under Exclusion Criteria**. 17. **Added** "(*Hypericum perforatum*)" **under Exclusion Criteria** to table under "Coadministration of Harvoni® with…", line entitled "Herbal Supplements". 18. **Added** "Mavyret™ (glecaprevir/pibrentasvir)" **and** "Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)" **under Exclusion Criteria** to table under "Coadministration of Harvoni® with…", line entitled "NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection". 19. **Changed table below Authorization under Approval Length from (changes made highlighted in**

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yellow):

Drug Therapy	Cirrhosis	G1a		G1b		G4		G5		G6	
		TN	TE	TN	TE	TN	TE	TN	TE	TN	TE
Harvoni®	No	12w	12w[5]	12w	12w[5]	12w	12w[1]	12w	12w[1]	12w	12w[1]
	No & low HCV RNA[*]	8w[*]		8w[*]							
	No & Post Transplant[^]	24w[^]		24w[^]		24w[^]					
	Comp	12w	24w[5]	12w	24w[5]	12w	24w[1]	12w	12w[1]	12w	12w[1]
	Comp & Post Transplant[^]	24w[^]		24w[^]		24w[^]					
	Decomp	24w	24w	24w	24w	24w	24w				
Harvoni® + RBV	No		12w[3]		12w[3]						
	No & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]				
	Comp		12w[5], 24w[3]		12w[5], 24w[3]		12w[1]				
	Comp & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]				
	Decomp	12w	12w[5]	12w	12w[5]	12w	12w				
	Decomp & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]				

TN = treatment naïve; TE = treatment experienced; Comp = compensated; Decomp = decompensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks

[*]Harvoni® for 8 weeks may be considered in G1 treatment-naïve patients without cirrhosis who have a pre-treatment HCV RNA < 6 million IU/ml.

[^]For patients who develop HCV infection post-liver transplantation.

[1]For patients who have failed pegIFN/RBV.

[3]For patients who have failed sofosbuvir + RBV +/- pegIFN.

[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.

to:

Drug Therapy	Cirrhosis	G1a		G1b		G4		G5		G6	
		TN	TE	TN	TE	TN	TE	TN	TE	TN	T
Harvoni®	No	12w	12w[5]	12w	12w[5]	12w	12w[1]	12w	12w[1]	12w	1
	No & low HCV RNA[*]	8w[*]		8w[*]							
	Comp	12w	24w[5]	12w	24w[5]	12w	12w[1]	12w	12w[1]	12w	1
	Decomp	24w		24w		24w		24w		24w	
Harvoni® +	No		12w[9x]		12w[9x]						

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	RBV	No & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^
		Comp		12w[5]		12w[5]		12w[1]				
		Comp & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^
		Decomp	12w	24w[11]	12w	24w[11]	12w	24w[11]	12w	24w[11]	12w	24w[11]
		Decomp & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^	12w^

TN = treatment naïve; TE = treatment experienced; Comp = compensated; Decomp = decompensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks

[x]Except in patients who have failed simeprevir.

[*]Harvoni® for 8 weeks may be considered in G1 treatment-naïve patients without cirrhosis who are non-black, HIV-uninfected, and have a pre-treatment HCV RNA < 6 million IU/ml.

^For patients who develop HCV infection post-liver transplantation.

[1]For patients who have failed pegIFN/RBV.

[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.

[9]For patients who have failed a non-NS5A inhibitor, sofosbuvir-containing regimen.

[11]For patients who failed a sofosbuvir-based treatment only.

7/30/2016	1. **Changed** "Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/dasabuvir)" **to** "Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir)" in list of drugs following the statement "As retreatment when there has been relapse after, or no response to, a prior treatment course with…" **under Exclusion Criteria**. 2. **Changed** "Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/dasabuvir)" **to** "Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir)" **under Exclusion Criteria** to table under "Coadministration of Harvoni® with…", line entitled "NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection".
7/21/2016	1. **Changed** "IV. A. 1. Patient has a documented contraindication to Zepatier™" **to** "IV. A. 1. Patient meets ALL of criteria a through c below: a. Patient has a documented contraindication to Zepatier™; b. Patient meets ONE of criteria i or ii: i. Patient has a documented contraindication to Epclusa®; ii. Patient is treatment-naïve without cirrhosis and has a pre-treatment HCV RNA < 6 million IU/ml); c. Patient meets ONE of criteria i, ii, or iii: i. Patient does not have cirrhosis; ii. Patient has compensated cirrhosis, but has not failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir); iii. If patient has compensated cirrhosis, and has failed prior treatment with peginterferon + ribavirin +/- a NS3 protease inhibitor (telaprevir, boceprevir, or simeprevir), then patient must also meet ONE of criteria aa or bb: aa. Harvoni® is prescribed in combination with ribavirin; Patient has a documented intolerance or contraindication to ribavirin" **under Prior Authorization Criteria**. 2. **Changed** "IV. A. 2. Patient has decompensated cirrhosis (Child-Pugh B or C)" **to** "IV. A. 2. Patient has decompensated cirrhosis (Child-Pugh B) AND meets BOTH of criteria a and b: a. Patient has a documented contraindication to Epclusa®; b. Patient meets ONE of criteria i or ii: i. Harvoni® is prescribed in combination with ribavirin; ii. Patient has a documented intolerance or contraindication to ribavirin" **under Prior Authorization Criteria**. 3. **Changed** "IV. A. 3. Patient is post-liver transplant" **to** "IV. A. 3. Patient is post-liver transplant and meets ONE of criteria a or b: a. Harvoni® is prescribed in combination with ribavirin; b. Patient has a documented intolerance or contraindication to ribavirin" **under Prior Authorization Criteria**. 4. **Changed** "IV. B. 1. Patient has a documented contraindication to Zepatier™" **to** "1. Patient meets BOTH of criteria a and b below: a. Patient has a documented contraindication to Zepatier™ and Epclusa®; b. Patient meets ONE of criteria i, ii, or iii: i. Patient does not have cirrhosis; ii. Patient has compensated cirrhosis, but

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has not failed prior treatment with peginterferon + ribavirin; iii. If patient has compensated cirrhosis, and has failed prior treatment with peginterferon + ribavirin, then patient must also meet ONE of criteria aa or bb: aa. Harvoni® is prescribed in combination with ribavirin; bb. Patient has a documented intolerance or contraindication to ribavirin" **under Prior Authorization Criteria**.

5. **Changed** "IV. B. 2. Patient has decompensated cirrhosis (Child-Pugh B or C)" **to** "IV. B. 2. Patient has decompensated cirrhosis (Child-Pugh B) and AND meets BOTH of criteria a and b: a. Patient has a documented contraindication to Epclusa®; b. Patient meets ONE of criteria i or ii: i. Harvoni® is prescribed in combination with ribavirin; ii. Patient has a documented intolerance or contraindication to ribavirin" **under Prior Authorization Criteria**.
6. **Changed** "IV. B. 3. Patient is post-liver transplant" **to** "IV. B. 3. Patient is post-liver transplant and meets ONE of criteria a or b: a. Harvoni® is prescribed in combination with ribavirin; b. Patient has a documented intolerance or contraindication to ribavirin" **under Prior Authorization Criteria**.
7. **Changed** "IV. C. Patient has genotypes 5 or 6" **to** "IV. C. Patient has genotypes 5 or 6 and criterion 1 is met: 1. Patient has a documented contraindication Epclusa®" **under Prior Authorization Criteria**.
8. **Added** "Child-Pugh C" **under Exclusion Criteria**.
9. **Changed** "Coadministration of Harvoni® with any of the drugs listed in the table below…" **to** "Coadministration of Harvoni® with P-gp inducers or any of the drugs listed in the table below…' **under Exclusion Criteria**.
10. **Added** "Epclusa® (sofosbuvir/velpatasvir)" **under Exclusion Criteria** to: 1) List of drugs following the statement "As retreatment when there has been relapse after, or no response to, a prior treatment course with…; 2) table under "Coadministration of Harvoni® with …", line entitled "NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection".
11. **Added** "(elbasvir/grazoprevir)" following Zepatier™ **under Exclusion Criteria** to table under "Coadministration of Harvoni® with …", line entitled "NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection".
12. **Changed table below Authorization under Approval Length from (changes made highlighted in yellow):**

Drug Therapy	**Cirrhosis**	**Authorization Duration**									
		G1a		**G1b**		**G4**		**G5**		**G6**	
		TN	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**
Harvoni®	No	12w	12w[5]	12w	12w[5]	12w	12w[1]	12w	12w[1]	12w	12w[1]
	No & low HCV RNA*	8w*		8w*							
	No & Post Transplant^	24w^		24w^		24w^					
	Comp	12w	24w[5]	12w	24w[5]	12w	24w[1]	12w	12w[1]	12w	12w[1]
	Comp & Post Transplant^	24w^		24w^		24w^					
	Decomp	24w		24w		24w					
Harvoni® + RBV	No		12w[3]		12w[3]						
	No & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^				
	Comp		12w[5], 24w[3]		12w[5], 24w[3]		12w[1]				
	Comp & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^				
	Decomp	12w	12w[5],	12w	12w[5],	12w	24w[6]				

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			24w[6]		24w[6]						
	Decomp & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^				

TN = treatment naïve; TE = treatment experienced; Comp = compensated; Decomp = decompensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks
*Harvoni® for 8 weeks may be considered in G1 treatment-naïve patients without cirrhosis who have a pre-treatment HCV RNA < 6 million IU/ml.
^For patients who develop HCV infection post-liver transplantation.
[1]For patients who have failed pegIFN/RBV.
[3]For patients who have failed sofosbuvir + RBV +/- pegIFN.
[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.
[6]For patients who have failed a sofosbuvir-based treatment.

to:

Drug Therapy	**Cirrhosis**	**G1a**		**G1b**		**G4**		**G5**		**G6**	
		TN	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**
Harvoni®	No	12w	12w[5]	12w	12w[5]	12w	12w[1]	12w	12w[1]	12w	12w[1]
	No & low HCV RNA*	8w*		8w*							
	No & Post Transplant^	24w^		24w^		24w^					
	Comp	12w	24w[5]	12w	24w[5]	12w	24w[1]	12w	12w[1]	12w	12w[1]
	Comp & Post Transplant^	24w^		24w^		24w^					
	Decomp	24w	24w	24w	24w	24w	24w				
Harvoni® + RBV	No		12w[3]		12w[3]						
	No & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^				
	Comp		12w[5], 24w[3]		12w[5], 24w[3]		12w[1]				
	Comp & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^				
	Decomp	12w	12w[5]	12w	12w[5]	12w	12w				
	Decomp & Post Transplant^	12w^	12w^	12w^	12w^	12w^	12w^				

TN = treatment naïve; TE = treatment experienced; Comp = compensated; Decomp = decompensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks
*Harvoni® for 8 weeks may be considered in G1 treatment-naïve patients without cirrhosis who have a pre-treatment HCV RNA < 6 million IU/ml.
^For patients who develop HCV infection post-liver transplantation.
[1]For patients who have failed pegIFN/RBV.

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<table>
<tr><td colspan="2">Historical Tracking Of Changes Made To Policy</td></tr>
<tr><td></td><td>[3]For patients who have failed sofosbuvir + RBV +/- pegIFN.
[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.
13. Updated “http://www.bcbsnc.com/assets/services/public/pdfs/formulary/harvoni_criteria.pdf” to “http://www.bcbsnc.com/assets/services/public/pdfs/formulary/Harvoni_UM_Criteria.pdf” under References.</td></tr>
<tr><td>3/21/2016</td><td>1. Changed “member” to “patient” throughout policy.
2. Changed “III. Documentation of member’s Hepatitis C treatment history and baseline viral load and ONE of the following criteria A or B must be met: A. Member is treatment-naïve; B. Member has failed prior treatment with one of the following 1, 2, or 3 AND meets criteria listed under applicable failed treatment: 1. Peginterferon + ribavirin +/- protease inhibitor AND one of criteria a or b is met: a. Member has Genotype 1 without cirrhosis OR has Genotype 4, 5, or 6; b. Member has Genotype 1 with cirrhosis and meets ONE of the following i or ii: i Harvoni® is used in combination with ribavirin; ii Member has a documented intolerance or contraindication to ribavirin; 2. Sovaldi® + Olysio® AND criteria a and b are met: a. Member has Genotype 1; b. Harvoni® is used in combination with ribavirin; 3. Sovaldi® + ribavirin +/- peginterferon AND criteria a and b are met: a. Member has Genotype 1; b. Harvoni® is used in combination with ribavirin” to “III. Documentation of patient’s Hepatitis C treatment history and baseline viral load; IV. Documentation that patient meets ONE of the following criteria A through C: A. Patient has genotype 1 AND meets ONE of criteria 1 through 4: 1. Patient has a documented contraindication to Zepatier™; 2. Patient has decompensated cirrhosis (Child-Pugh B or C); 3. Patient is post-liver transplant; 4. Patient has failed prior treatment with Sovaldi® + ribavirin +/- peginterferon; B. Patient has genotype 4 AND meets ONE of criteria 1 through 3: 1. Patient has a documented contraindication to Zepatier™; 2. Patient has decompensated cirrhosis (Child-Pugh B or C); 3. Patient is post-liver transplant; C. Patient has genotypes 5 or 6; V. Documentation that patient's hepatitis C drug therapy is prescribed as outlined in the table under Authorization in the Approval Length section” under Prior Authorization Criteria.
3. Changed “As retreatment when there has been relapse after, or no response to, a prior treatment course with Daklinza™ (daclatasvir), Harvoni® (ledipasvir/sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), or Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/dasabuvir)” to “As retreatment when there has been relapse after, or no response to, a prior treatment course with Daklinza™ (daclatasvir), Harvoni® (ledipasvir/sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/dasabuvir), or Zepatier™ (elbasvir/grazoprevir)” under Exclusion Criteria.
4. Added “Zepatier™” to “NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection” line on table underneath Exclusion Criteria.
5. Changed “http://www.hcvguidelines.org/fullreport” to “http://hcvguidelines.org/full-report-view” under References.
6. Changed table following Authorization under Approval Length from:
<table>
<tr><th colspan="2">Patient Characteristics</th><th colspan="2">Authorization Information</th></tr>
<tr><th>Genotype, Other Features</th><th>Hepatitis Treatment History</th><th>Treatment</th><th>Authorization Duration</th></tr>
<tr><td>1a or 1b, without cirrhosis</td><td>Treatment-naïve/ Treatment-experienced (failed peginterferon + ribavirin +/- protease inhibitor)</td><td>Harvoni®</td><td>12 weeks</td></tr>
<tr><td>1a or 1b, without cirrhosis</td><td>Treatment-experienced (failed:
1. Sovaldi® + ribavirin +/- peginterferon, OR
2. Olysio® + Sovaldi®)</td><td>Harvoni® + ribavirin</td><td>12 weeks</td></tr>
</table></td></tr>
</table>

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1a or 1b, with cirrhosis	Treatment-naïve	Harvoni®	**12 weeks**
1a or 1b, with cirrhosis	Treatment-experienced *(failed peginterferon + ribavirin +/- protease inhibitor)*	Harvoni® + ribavirin	**12 weeks**
		Harvoni®	**24 weeks**
1a or 1b, with cirrhosis	Treatment-experienced *(failed: 1. Sovaldi® + ribavirin +/- peginterferon, OR 2. Olysio® + Sovaldi®)*	Harvoni® + ribavirin	**24 weeks**
4, 5, or 6	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin +/- protease inhibitor)*	Harvoni®	**12 weeks**

to:

Drug Therapy	**Cirrhosis**	**Authorization Duration**									
		G1a		**G1b**		**G4**		**G5**		**G6**	
		TN	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**
Harvoni®	No	12w	12w[5]	12w	12w[5]	12w	12w[1]	12w	12w[1]	12w	12w[1]
	No & low HCV RNA[*]	8w[*]		8w[*]							
	No & Post Transplant[^]	24w[^]		24w[^]		24w[^]					
	Comp	12w	24w[5]	12w	24w[5]	12w	24w[1]	12w	12w[1]	12w	12w[1]
	Comp & Post Transplant[^]	24w[^]		24w[^]		24w[^]					
	Decomp	24w		24w		24w					
Harvoni® + RBV	No		12w[3]		12w[3]						
	No & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]				
	Comp		12w[5], 24w[3]		12w[5], 24w[3]		12w[1]				
	Comp & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]				
	Decomp	12w	12w[5], 24w[6]	12w	12w[5], 24w[6]	12w	24w[6]				
	Decomp & Post Transplant[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]	12w[^]				

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	TN = treatment naïve; TE = treatment experienced; Comp = compensated; Decomp = decompensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks *Harvoni® for 8 weeks may be considered in G1 treatment-naïve patients without cirrhosis who have a pre-treatment HCV RNA < 6 million IU/ml. ^For patients who develop HCV infection post-liver transplantation. [1]For patients who have failed pegIFN/RBV. [3]For patients who have failed sofosbuvir + RBV +/- pegIFN. [5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor. [6]For patients who have failed a sofosbuvir-based treatment.
12/7/2015	1. **Changed** "Documented diagnosis of chronic hepatitis C (CHC) genotypes 1, 4, or 6 infection" **to** "Documented diagnosis of chronic hepatitis C (CHC) genotypes 1, 4, 5, or 6 infection" **under Prior Authorization Criteria**. 2. **Changed** "III. Documentation of member's Hepatitis C treatment history and baseline viral load" **to** "III. Documentation of member's Hepatitis C treatment history and baseline viral load and ONE of the following criteria A or B must be met: A. Member is treatment-naïve; B. Member has failed prior treatment with one of the following 1, 2, or 3 AND meets criteria listed under applicable failed treatment: 1. Peginterferon + ribavirin +/- protease inhibitor AND one of criteria a or b is met: a. Member has Genotype 1 without cirrhosis OR has Genotype 4, 5, or 6; b. Member has Genotype 1 with cirrhosis and meets ONE of the following i or ii: i Harvoni® is used in combination with ribavirin; ii. Member has a documented intolerance or contraindication to ribavirin; 2. Sovaldi® + Olysio® AND criteria a and b are met: a. Member has Genotype 1; b. Harvoni® is used in combination with ribavirin; 3. Sovaldi® + ribavirin +/- peginterferon AND criteria a and b are met: a. Member has Genotype 1; b. Harvoni® is used in combination with ribavirin" **under Prior Authorization Criteria**. 3. **Changed** "As retreatment when there has been relapse after, or no response to, a prior treatment course with Harvoni® (ledipasvir/sofosbuvir), Sovaldi® (sofosbuvir), or Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir /dasabuvir)" **to** "As retreatment when there has been relapse after, or no response to, a prior treatment course with Daklinza™ (daclatasvir), Harvoni® (ledipasvir/sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), or Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/dasabuvir)" **under Exclusion Criteria**. 4. **Changed:** Other polymerase inhibitors or protease inhibitors used to treat chronic hepatitis C virus infection — Olysio® (simeprevir), Sovaldi® (sofosbuvir), Victrelis® (boceprevir), Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir /dasabuvir) **to:** NS5A inhibitors, polymerase inhibitors, or protease inhibitors used to treat chronic hepatitis C virus infection — Daklinza™ (daclatasvir), Olysio® (simeprevir), Sovaldi® (sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Victrelis® (boceprevir), Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/dasabuvir) **on table under Exclusion Criteria**. 5. **Changed:**

Genotype	Patient Characteristics	Authorization Duration
1	Treatment-naïve without cirrhosis, and pre-treatment HCV RNA < 6 million IU/mL	**8 weeks**
1	Treatment-naïve without cirrhosis, and pre-treatment HCV RNA ≥ 6 million IU/mL	**12 weeks**
1	Treatment-naïve with cirrhosis	**12 weeks**

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1	Treatment-experienced without cirrhosis	**12 weeks**
1	Treatment-experienced with cirrhosis, and used in combination with ribavirin	**12 weeks**
1	Treatment-experienced with cirrhosis	**24 weeks**
4	Treatment-naïve or treatment-experienced	**12 weeks**
6	Treatment-naïve or treatment-experienced	**12 weeks**

to:

Patient Characteristics		**Authorization Information**	
Genotype, Other Features	**Hepatitis Treatment History**	**Treatment**	**Authorization Duration**
1a or 1b, without cirrhosis	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin +/- protease inhibitor)*	Harvoni®	**12 weeks**
1a or 1b, without cirrhosis	Treatment-experienced *(failed: 1. Sovaldi® + ribavirin +/- peginterferon, OR 2. Olysio® + Sovaldi®)*	Harvoni® + ribavirin	**12 weeks**
1a or 1b, with cirrhosis	Treatment-naïve	Harvoni®	**12 weeks**
1a or 1b, with cirrhosis	Treatment-experienced *(failed peginterferon + ribavirin +/- protease inhibitor)*	Harvoni® + ribavirin	**12 weeks**
		Harvoni®	**24 weeks**
1a or 1b, with cirrhosis	Treatment-experienced *(failed: 1. Sovaldi® + ribavirin +/- peginterferon, OR 2. Olysio® + Sovaldi®)*	Harvoni® + ribavirin	**24 weeks**
4, 5, or 6	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin +/- protease inhibitor)*	Harvoni®	**12 weeks**

on table following Authorization under Approval Length.

5/20/2015	1. **Changed** "II. Documentation that member meets ONE of the following criteria A through I: A. Has a Metavir score of F2 (fibrosis), F3 (advanced fibrosis), or F4 (compensated cirrhosis); B. Is post-liver transplant; C. Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2: 1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis); 2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis; D. Is coinfected with HIV-1; E. Is coinfected with Hepatitis B virus (HBV); F. Has other coexistent liver disease [i.e. nonalcoholic steatohepatitis (NASH)]; G. Has debilitating fatigue as evidenced by the documentation of significant limitations of instrumental activities of daily living (i.e. meal preparation, household chores, etc.);

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	H. Has Type 2 diabetes mellitus (insulin resistant); I. Has porphyria cutanea tarda" **to** "II. Documentation that member meets ONE of the following criteria A, B, or C: A. Has a Metavir score of F3 (advanced fibrosis) or F4 (compensated cirrhosis); B. Is post-liver transplant; C. Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2: 1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis); 2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis" **under Prior Authorization Criteria**.
4/1/2015	1. **Changed** "II. Documentation that member meets ONE of the following criteria A, B, or C: A. Has a Metavir score of F3 (advanced fibrosis) or F4 (compensated cirrhosis); B. Is post-liver transplant; C. Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2: 1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis); 2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis." **to** "II. Documentation that member meets ONE of the following criteria A through I: A. Has a Metavir score of F2 (fibrosis), F3 (advanced fibrosis), or F4 (compensated cirrhosis); B. Is post-liver transplant; C. Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2: 1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis); 2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis; D. Is coinfected with HIV-1; E. Is coinfected with Hepatitis B virus (HBV); F. Has other coexistent liver disease [i.e. nonalcoholic steatohepatitis (NASH)]; G. Has debilitating fatigue as evidenced by the documentation of significant limitations of instrumental activities of daily living (i.e. meal preparation, household chores, etc.); H. Has Type 2 diabetes mellitus (insulin resistant); I. Has porphyria cutanea tarda" **under Prior Authorization Criteria**.
3/25/2015	1. **Added** "Antiarrhythmics: Amiodarone" **on table for "Coadministration of Harvoni® with any of drugs listed in the table below" under Exclusion Criteria**. 2. **Added** "1: Treatment-experienced with cirrhosis, and used in combination with ribavirin: 12 weeks" for Genotype, Patient Characteristics, and Authorization Duration **on table under Approval Length**. 3. **Added** "http://www.fda.gov/Drugs/DrugSafety/ucm439484.htm" **under References**.
2/8/2015	1. **Changed** "Documented diagnosis of chronic hepatitis C (CHC) genotypes 1 or 6 infection" **to** "Documented diagnosis of chronic hepatitis C (CHC) genotypes 1, 4, or 6 infection" **under Prior Authorization Criteria**. 2. **Added** "Genotype 4: Treatment-naïve or treatment-experienced; 12 weeks" **to table under Approval Length section**.
2/7/2015	1. **Changed** "P-gp inducers: Rifampin, St. John's wort" **to** "Herbal Supplements: St. John's wort" **on table for "Coadministration of Harvoni® with any of drugs listed in the table below" under Exclusion Criteria**.
1/28/2015	1. **Changed** "Documented diagnosis of chronic hepatitis C (CHC) genotype 1 infection" **to** "Documented diagnosis of chronic hepatitis C (CHC) genotypes 1 or 6 infection" **under Prior Authorization Criteria**. 2. **Changed** "Has serious extrahepatic manifestations of hepatitis C infection" **to** "Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2: 1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis); 2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis" **under Prior Authorization Criteria**. 3. **Changed** "Documentation of member's treatment history (i.e. treatment-naïve or treatment-experienced)" **to** "Documentation of member's Hepatitis C treatment history" **under Prior Authorization Criteria**. 4. **Removed** "Documentation that the member has not attempted a previous course of therapy with sofosbuvir" **from Prior Authorization Criteria, and added** "As retreatment when there has been relapse after, or no response to, a prior treatment course with Harvoni® (ledipasvir/sofosbuvir), Sovaldi® (sofosbuvir), or Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir /dasabuvir)" **to Exclusion Criteria**. 5. **Changed** "Coadministered of Harvoni® with any of drugs listed in the table below:" **to** "Coadministration of Harvoni® with any of the drugs listed in the table below:" **under Exclusion Criteria**. 6. **Changed** "Other direct-acting antivirals used to treat CHC: Olysio™ (simeprevir), Victrelis® (boceprevir)]; Other drugs containing sofosbuvir: Sovaldi®" **to** "Other polymerase inhibitors or protease inhibitors used to treat chronic hepatitis C virus infection: Olysio® (simeprevir), Sovaldi® (sofosbuvir), Victrelis®

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	(boceprevir), Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir /dasabuvir)" **on table for "Coadministration of Harvoni® with any of drugs listed in the table below" under Exclusion Criteria**. 7. **Added** Genotype column and row for Genotype 6 **on table under Approval Length**. 8. **Updated** "http://www.hcvguidelines.org/sites/default/files/full_report.pdf" **to** "http://www.hcvguidelines.org/fullreport" **and "**http://www.bcbsnc.com/assets/services/public/pdfs/formulary/harvoni_um_criteria.pdf" **to** "http://www.bcbsnc.com/assets/services/public/pdfs/formulary/harvoni_criteria.pdf"**under References**. 9. **Added** "http://blue.regence.com/trgmedpol/drugs/dru366.pdf" **under References**.