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Subject: Hepatitis C Drug Therapy

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Position Statement	Dosage/ Administration	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Hepatitis C virus (HCV) is one of the leading causes of chronic liver disease in the United States. It is estimated that 3.9 million Americans have been infected with HCV with chronic liver disease developing in about 70% of the cases. About 1 – 5% of chronic liver disease cases due to HCV may die and HCV liver disease is the leading indication for liver transplants. The primary source for HCV infection is due to exposure to infected blood or blood products.

Currently the treatment of choice for chronic HCV infection in compensated liver disease is combination therapy. There are 6 major HCV genotypes, which predict treatment response. The majority of drug therapy data is dedicated to treating genotypes 1 – 4.

Production of hepatitis C protease inhibitors telaprevir (Incivek) and boceprevir (Victrelis) have been discontinued as of October 2014 and December 2015, respectively. In May 2018, AbbVie announced Technivie, Viekira Pak, and Viekira XR would be withdrawn from the US market in January 2019. Product will remain available through the end of 2018 to allow for current users to finish treatment. AbbVie has recommended that no new patients start treatment with Technivie, Viekira Pak, or Viekira XR beginning July 2018.

POSITION STATEMENT

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

NOTE:

- **Glecaprevir-Pibrentasvir (Mavyret™), Ledipasvir-Sofosbuvir (Harvoni®), Sofosbuvir-Velpatasvir (Epclusa®), and Sofosbuvir-Velpatasvir-Voxilaprevir (Vosevi™) are the preferred direct acting antiviral products.**
- Approval duration is based on genotype, treatment regimen, ribavirin and/or interferon eligibility, prior treatment (including treatment failures), baseline HCV RNA, transplant status, and number of doses receieved of requested regimen

Initiation of hepatitis C drug therapy **meets the definition of medical necessity** when all of the following criteria are met:

1. Indication for use is treatment of chronic hepatitis C
2. Laboratory documentation of HCV genotype is provided
3. Laboratory documentation of baseline HCV viral RNA is provided
4. Treatment is prescribed or supervised by a gastroenterologist, hepatologist, or infectious disease or transplant physician with the following exceptions:
    a. If coinfection with HIV, treatment must be prescribed or supervised by an infectious disease physician
    b. If diagnosis of hepatocellular carcinoma (and transplant eligible), awaiting liver transplantation, or post-liver transplantation, treatment must be prescribed or supervised by a transplant physician
5. Member meets **ONE** of the following:
    a. Documentation of fibrosis severity is provided as any of the following:
        i. Indirect serum biomarkers – laboratory documentation must be provided
        ii. Direct serum biomarkers – laboratory documentation must be provided
        iii. Fibroscan or similar elastographic devices – laboratory documentation must be provided
        iv. Liver biopsy – laboratory documentation must be provided
    b. Documentation of cirrhosis is provided as any of the following:
        i. Indirect serum biomarkers – laboratory documentation must be provided
        ii. Direct serum biomarkers – laboratory documentation must be provided
        iii. Fibroscan or similar elastographic devices – laboratory documentation must be provided
        iv. Liver biopsy – laboratory documentation must be provided
    c. Diagnosed with hepatocellular carcinoma awaiting liver transplantation – documentation from the medical record must be provided
    d. Liver transplant recipient – documentation from the medical record must be provided

6. Both the member and prescriber agree to provide documentation of virological response (i.e., HCV viral RNA level) upon completion of therapy
7. Member meets product specific criteria outlined in Table 1
8. Hepatitis C drug therapy does not exceed the maximum treatment duration for the requested regimen (see Table 2)

Continuation of hepatitis C drug therapy meets the definition of **medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan, **OR** the member previously met all initiation criteria
2. Continuation of hepatitis C drug therapy does not exceed the maximum treatment duration for the requested regimen (see Table 2)

   NOTE: Continuation of hepatitis C drug therapy will account for the number of doses the member has already received.

Approval duration: See Table 2

Table 1

Initiation criteria for use of hepatitis C drug therapy	
Product *Brand*	**Criteria**
Daclatasvir *Daklinza*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 2, 3, or 4 2. Use is in combination with **ONE** of the following: a. sofosbuvir (Sovaldi)* b. sofosbuvir (Sovaldi)* **AND** ribavirin 3. Member has a contraindication to treatment with each of the following direct acting antivirals (specific contraindication must be provided): a. glecaprevir-pibrentasvir (Mavyret) b. ledipasvir-sofosbuvir (Harvoni) – genotype 1 and 4 **ONLY** c. sofosbuvir-velpatasvir (Epclusa) d. sofosbuvir-velpatasvir-voxilaprevir (Vosevi) 4. Member meets one of the following: a. Total daily dose does not exceed 60 mg b. Total daily dose does not exceed 90 mg AND daclatasvir is coadministered with a moderate CYP3A inducer (e.g., bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin,

	rifapentine) or nevirapine Approval duration: See Table 2
Elbasvir-Grazoprevir *Zepatier*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 3, or 4 2. Use is alone (i.e., not in combination with any other hepatitis C therapy) **OR** in combination with **ONE** of the following: a. ribavirin b. sofosbuvir (Sovaldi)* – genotype 3 **ONLY** 3. Member has a contraindication to treatment with each of the following direct acting antivirals (specific contraindication must be provided): a. glecaprevir-pibrentasvir (Mavyret) b. ledipasvir-sofosbuvir (Harvoni) c. sofosbuvir-velpatasvir (Epclusa) d. sofosbuvir-velpatasvir-voxilaprevir (Vosevi) 4. Total daily dose does not exceed one tablet (elbasvir 50 mg-grazoprevir 100 mg) Approval duration: See Table 2
Glecaprevir-Pibrentasvir *Mavyret*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 2, 3, 4, 5, or 6 2. Use is alone (i.e., not in combination with any other hepatitis C therapy) 3. Total daily dose does not exceed three tablets (glecaprevir 100 mg-vpibrentasvir 40 mg) Approval duration: See Table 2
Ledipasvir-Sofosbuvir *Harvoni*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 4, 5, or 6 2. Member does not have severe renal impairment or end stage renal disease (estimated Glomerular Filtration Rate less than 30 mL/min/1.73m2) – laboratory documentation of recent (i.e., within 6 months) serum creatinine must be provided 3. Use is alone (i.e., not in combination with any other hepatitis C therapy) **OR** in combination with ribavirin 4. Total daily dose does not exceed one tablet (ledipasvir 90 mg-sofosbuvir 400 mg-)

	Approval duration: See Table 2
Ombitasvir-paritaprevir-ritonavir *Technivie*	Use is **not a medical necessity.**
Ombitasvir-paritaprevir-ritonavir; dasabuvir *Viekira Pak, Viekira XR*	Use is **not a medical necessity.**
Simeprevir *Olysio*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1 2. Member does not have HCV genotype 1a with NS3 Q80K polymorphism 3. Use is in combination with sofosbuvir (Sovaldi)* 4. Member has not previously been treated with telaprevir or boceprevir 5. Member has a contraindication to treatment with each of the following direct acting antivirals (specific contraindication must be provided): a. glecaprevir-pibrentasvir (Mavyret) b. ledipasvir-sofosbuvir (Harvoni) – genotype 1 and 4 **ONLY** c. sofosbuvir-velpatasvir (Epclusa) d. sofosbuvir-velpatasvir-voxilaprevir (Vosevi) 6. Total daily dose does not exceed 150 mg Approval duration: See Table 2
Sofosbuvir *Sovaldi*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 2, 3, 4, 5 or 6 2. Member does not have severe renal impairment or end stage renal disease (estimated Glomerular Filtration Rate less than 30 mL/min/1.73m2) – laboratory documentation of recent (i.e., within 6 months) serum creatinine must be provided 3. Use is in combination with **ONE** of the following: a. daclatasvir (Daklinza)***** b. daclatasvir (Daklinza)*** AND** ribavirin

	c. elbasvir-grazoprevir (Zepatier)* - genotype 3 **ONLY** d. simeprevir (Olysio)* 4. Total daily dose does not exceed 400 mg Approval duration: See Table 2
Sofosbuvir-Velpatasvir *Epclusa*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 2, 3, 4, 5, or 6 2. Member does not have severe renal impairment or end stage renal disease (estimated Glomerular Filtration Rate less than 30 mL/min/1.73m2) – laboratory documentation of recent (i.e., within 6 months) serum creatinine must be provided 3. Use is alone (i.e., not in combination with any other hepatitis C therapy) **OR** in combination with ribavirin 4. Total daily dose does not exceed one tablet (sofosbuvir 400 mg-velpatasvir 100 mg) Approval duration: See Table 2
Sofosbuvir-Velpatasvir-Voxilaprevir *Vosevi*	Use is a **medical necessity** when **ALL** criteria are met: 1. Member has a laboratory confirmed HCV genotype 1, 2, 3, 4, 5, or 6 2. Member does not have severe renal impairment or end stage renal disease (estimated Glomerular Filtration Rate less than 30 mL/min/1.73m2) – laboratory documentation of recent (i.e., within 6 months) serum creatinine must be provided 3. Use is alone (i.e., not in combination with any other hepatitis C therapy) **OR** in combination with ribavirin 4. Total daily dose does not exceed one tablet (sofosbuvir 400 mg-velpatasvir 100 mg-voxilaprevir 100 mg) Approval duration: See Table 2
* Prior authorization required. Member must meet prior authorization criteria for **ALL** prescribed agents to be approved for combination therapy with the requested agent.	

Table 2

NOTE:

- **Glecaprevir-Pibrentasvir (Mavyret™), Ledipasvir-Sofosbuvir (Harvoni®), Sofosbuvir-Velpatasvir (Epclusa®), and Sofosbuvir-Velpatasvir-Voxilaprevir (Vosevi™) are the preferred direct acting antiviral products.**
- Approval duration will account for any doses received since initiation of treatment.

Table 2: Maximum treatment/duration of approval for hepatitis C drug therapy

Genotype	Cirrhosis	Regimen	Required (ALL must be met for desired regimen)	Maximum Approval Duration
1	Absent	**Daklinza + Sovaldi**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Epclusa† (or authorized generic)	• Treatment naïve	12 weeks
			• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve • Non-black AND HIV-negative • Pre-treatment HCV RNA less than 6 million IU/mL	8 weeks
			• Treatment naïve • Black OR HIV-positive • Pre-treatment HCV RNA less than 6 million IU/mL or HIV/HCV-coinfection	12 weeks
			• Treatment naïve • Pre-treatment HCV RNA greater than 6 million IU/mL	12 weeks
			• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Harvoni† (or authorized generic) + RBV	• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced with PEG-IFN + RBV	8 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
			• Treatment experienced with simeprevir (Olysio) + sofosbuvir (Sovaldi)	12 weeks
			• Treatment experienced with PEG-IFN + RBV + HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir)	16 weeks
		Olysio + Sovaldi	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks

		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
			• Genotype 1a • Treatment experienced with simeprevir (Olysio) + sofosbuvir (Sovaldi) based regimen	12 weeks
		Zepatier	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Zepatier + RBV	• Treatment experienced with PEG-IFN + RBV + HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Genotype 1a with baseline NS5A RAS present • Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	16 weeks
	Post-liver transplant	**Harvoni† (or authorized generic) + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced	12 weeks
	Compensated	**Epclusa† (or authorized generic)**	• Treatment naïve	12 weeks
			• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve	12 weeks
		Harvoni† (or authorized generic) + RBV	• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
			• Treatment experienced with simeprevir (Olysio) + sofosbuvir (Sovaldi)	12 weeks
			• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir)	16 weeks

		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
		Zepatier	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Zepatier + RBV	• Genotype 1a with baseline NS5A RAS present • Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	16 weeks
			• Treatment experienced with PEG-IFN + RBV + HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
	Decompensated	**Daklinza + Sovaldi**	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir) • RBV contraindicated	24 weeks
		Daklinza + Sovaldi + RBV	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Epclusa† (or authorized generic)	• Treatment naïve or treatment experienced • RBV contraindicated	24 weeks
		Epclusa† (or authorized generic) + RBV	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with a sofosbuvir (Sovaldi)- or NS5A (e.g.,daclatasvir, elbasvir, ledipasvir, ombitasvir)-based regimen	24 weeks
		Harvoni† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir) • RBV contraindicated	24 weeks
		Harvoni† (or authorized generic)+ RBV	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir-based regimen	24 weeks
2	Absent	**Daklinza + Sovaldi**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Epclusa† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) + RBV +/- PEG-IFN	12 weeks

		Mavyret†	• Treatment naïve or treatment experienced with PEG-IFN + RBV	8 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) + RBV +/- PEG-IFN	12 weeks
		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
	Post-liver transplant	**Daklinza + Sovaldi + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced	12 weeks
	Compensated	**Daklinza + Sovaldi**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	24 weeks
		Epclusa† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) + RBV +/- PEG-IFN	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	12 weeks
			Treatment experienced with sofosbuvir (Sovaldi) + RBV +/- PEG-IFN	12 weeks
		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
	Decompensated	**Daklinza + Sovaldi + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Epclusa† (or authorized generic) + RBV	• Treatment naïve or treatment experienced	12 weeks
3	Absent	**Daklinza + Sovaldi**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Epclusa† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Mavyret†	• Treatment naïve	8 weeks
			• Treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	16 weeks
		Vosevi† +/- RBV	• Treatment experienced with PEG-IFN + RBV • Y93H substitution is present	12 weeks
			• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir,	12 weeks

			ombitasvir, or velpatasvir)	
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
	Post-liver transplant	**Daklinza + Sovaldi + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced	12 weeks
	Compensated	**Daklinza + Sovaldi + RBV**	• Treatment naïve or treatment experienced with sofosbuvir (Sovaldi) + RBV	24 weeks
		Daklinza + Sovaldi	• Treatment naïve • RBV contraindicated	24 weeks
		Epclusa† (or authorized generic)	• Treatment naïve	12 weeks
		Epclusa† (or authorized generic) + RBV	• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Mavyret†	• Treatment naïve	12 weeks
			• Treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	16 weeks
		Vosevi† +/- RBV	• Treatment naïve • Y93H substitution is present	12 weeks
			• Treatment experienced with PEG-IFN + RBV	12 weeks
			• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
			• Treatment experienced with sofosbuvir (Sovaldi) based regimen	12 weeks
		Zepatier + Sovaldi	• Treatment experienced with PEG-IFN + RBV	12 weeks
	Decompensated	**Daklinza + Sovaldi + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Epclusa† (or authorized generic) + RBV	• Treatment naïve or treatment experienced	12 weeks
4	Absent	**Epclusa† (or authorized generic)**	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	8 weeks

		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
		Zepatier	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Zepatier + RBV	• On-treatment virologic failure with PEG-IFN + RBV	16 weeks
	Post-liver transplant	**Harvoni† + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced	12 weeks
	Compensated	**Epclusa† (or authorized generic)**	• Treatment naïve	12 weeks
			• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve	12 weeks
		Harvoni† (or authorized generic) + RBV	• Treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	12 weeks
		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
		Zepatier	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Zepatier + RBV	• On-treatment virologic failure with PEG-IFN + RBV	16 weeks
	Decompensated	**Daklinza + Sovaldi**	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir) • RBV contraindicated	24 weeks
		Daklinza + Sovaldi + RBV	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
		Epclusa† (or authorized generic)	• Treatment naïve or treatment experienced • RBV contraindicated	24 weeks
		Epclusa† (or authorized	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks

		generic) + RBV	• Treatment experienced with a sofosbuvir (Sovaldi)- or NS5A (e.g.,daclatasvir, elbasvir, ledipasvir, ombitasvir)-based regimen	24 weeks
		Harvoni†	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir) • RBV contraindicated	24 weeks
		Harvoni† + RBV	• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- HCV protease inhibitor (telaprevir, boceprevir, simeprevir)	12 weeks
			• Treatment experienced with sofosbuvir-based regimen	24 weeks
5	Absent or Compensated	**Epclusa† (or authorized generic)**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Mavyret†	• No cirrhosis • Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	8 weeks
			• Compensated cirrhosis • Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	12 weeks
		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
	Post-liver transplant	**Harvoni† (or authorized generic) + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced	12 weeks
	Decompensated	**Epclusa† (or authorized generic)**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
6	Absent or Compensated	**Epclusa† (or authorized generic)**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Mavyret†	• No cirrhosis	8 weeks

			• Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	
			• Compensated cirrhosis • Treatment naïve or treatment experienced with PEG-IFN + RBV +/- sofosbuvir (Sovaldi)	12 weeks
		Vosevi†	• Treatment experienced with NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir)	12 weeks
	Post-liver transplant	**Harvoni† (or authorized generic) + RBV**	• Treatment naïve or treatment experienced	12 weeks
		Mavyret†	• Treatment naïve or treatment experienced	12 weeks
	Decompensated	**Epclusa† (or authorized generic)**	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
		Harvoni† (or authorized generic)	• Treatment naïve or treatment experienced with PEG-IFN + RBV	12 weeks
†Preferred direct-acting antiviral product PEG-IFN: peginterferon ; RAS: resistance-associated substitution; RBV: ribavirin;				

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Dosage and administration varies considerably between specific indications for use and treatment history. A brief overview of selected products is provided in Table 3, however it is strongly recommended that the prescriber refer to current guidelines and product-specific labeling for complete dosing and administration instructions.

Table 3

Dosage/Administration of hepatitis C drug therapy	
Product *Brand*	**Dosage/Administration**
Daclatasvir *Daklinza*	60 mg once daily (reduce to 30 mg once daily when coadminstered with strong CYP3A inhibitors; increase to 90 mg once daily when coadministered with moderate CYP3A inducers)Available as a 30 mg and 60 mg tablet
Elbasvir-Grazoprevir *Zepatier*	One tablet daily Available as 50 mg elbasvir-100 mg grazoprevir tablet

Glecaprevir-Pibrentasvir Mavyret	Three tablets once daily with food Available as 100 mg glecaprevir-40 mg pibrentasvir tablet
Ledipasvir-Sofosbuvir *Harvoni*	One tablet daily Available as a 90 mg ledipasivir-400 mg sofosbuvir tablet
Simeprevir *Olysio*	150 mg once daily with food Available as a 150 mg capsule
Sofosbuvir *Sovaldi*	400 mg once daily with food Available as a 400 mg capsule
Sofosbuvir-velpatasvir *Epclusa*	One tablet daily Available as a 400 mg sofosbuvir-100 mg velpatasvir tablet
Sofosbuvir-velpatasvir-voxilaprevir Vosevi	One tablet daily Available as a 400 mg sofosbuvir-100 mg velpatasvir-100 mg voxilaprevir tablet

PRECAUTIONS:

Specific precautions and warnings are highlighted in Table 4.

Table 4

Precautions and warnings of hepatitis C drug therapy	
Product *Brand*	**Precautions/Warnings**
Daclatasvir *Daklinza*	Contraindicated for co-administration with strong inducers of CYP3A
Elbasvir-Grazoprevir *Zepatier*	Contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C). Contraindicated for co-administration with OATP1B1/3 inhibitors, strong CYP3A inducers, and efavirenz.
Glecaprevir-Pibrentasvir Mavyret	Contraindicated in patients with severe hepatic impairment (Child-Pugh C) and for co-administration with atazanavir and rifampin
Ledipasvir-Sofosbuvir *Harvoni*	Bradycardia with amiodarone coadministration: Serious symptomatic bradycardia may occur in patients taking amiodarone, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone is not recommended. In patients without alternative, viable treatment options, cardiac monitoring is recommended. Use with P-gp inducers (e.g., rifampin, St. John's wort) may alter concentrations of ledipasvir and sofosbuvir
Simeprevir *Olysio*	Use has been associated with photosensitivity.
Sofosbuvir *Sovaldi*	Bradycardia with amiodarone coadministration: Serious symptomatic bradycardia may occur in patients taking amiodarone, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone is not recommended. In patients without alternative, viable treatment options, cardiac monitoring is recommended. Use with caution in combination with drugs that are potent P-gp inducers in the intestine (e.g., rifampin, St. John’s wort)
Sofosbuvir-velpatasvir	Bradycardia may occur in patients taking amiodarone, particularly in

Epclusa	patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone is not recommended. In patients without alternative viable treatment options, cardiac monitoring is recommended.
Sofosbuvir-velpatasvir-voxilaprevir Vosevi	Contraindicated for co-administration with rifampin. Bradycardia with amiodarone coadministration: Serious symptomatic bradycardia may occur in patients taking amiodarone, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone is not recommended. In patients without alternative, viable treatment options, cardiac monitoring is recommended.

BILLING/CODING INFORMATION:

HCPCS Coding:

J8499	Prescription drug, oral, non-chemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity:

B18.2	Chronic viral hepatitis C

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

DEFINITIONS:

Compensated liver disease: condition is stable and no clinical signs of physical or metabolic changes such as, but not limited to hepatic encephalopathy, variceal bleeding, ascites, acute changes in bilirubin, albumin, platelet count or bleeding time that cannot be not attributed to other organic cause(s).

Decompensated cirrhosis: moderate or severe hepatic impairment (Child Pugh class B or C)

Early Virological Response (EVR): a ≥ 2 log 10 reduction in HCV RNA level compared to baseline HCV RNA level (partial EVR) or HCV RNA negative at treatment week 12 (complete EVR).

Genotype: the genetic constitution of an organism or cell, as distinct from its expressed features or phenotype.

Hepatitis C virus: a viral infection caused by a single-stranded RNA virus of the family Flaviviridae (species Hepatitis C virus of the genus Hepacivirus) that tends to persist in the blood serum and is usually transmitted by infected blood (as by injection of an illicit drug, blood transfusion, or exposure to blood or blood products) and that accounts for most cases of chronic liver disease.

Null responder: those that fail to achieve a 2log10 HCV RNA decrease at week 24 of treatment.

Phenotype: the observable properties of an organism that are produced by the interaction of the genotype and the environment.

Rapid Virological Response (RVR): those that are HCV RNA negative at treatment week 4.

Responder: those that achieve an HCV RNA decrease greater than or equal to 2log10 by treatment week 12 followed by a sustained virological response (SVR) at the end of treatment.

Partial responder: those that achieve an HCV RNA decrease greater than or equal to 2log10 by treatment week 12, but fail to have a sustained virological response (SVR) at the end of treatment.

Poor interferon responder: those with less than 1 log 10 decline in viral load at treatment week 4.

Relapse: HCV RNA levels undetectable at end of treatment, but are detectable again at post treatment follow-up.

Sustained Virological Response (SVR): a negative HCV RNA level 24 weeks after cessation of treatment.

RELATED GUIDELINES:

None applicable.

OTHER:

Table 5: Metavir Fibrosis Scores	
F0	No fibrosis
F1	Portal fibrosis without septa
F2	Portal fibrosis with few septa
F3	Numerous septa without cirrhosis
F4	Cirrhosis

Table 6: Child Turcotte Pugh (CTP) classification of the severity of cirrhosis			
	Class A	Class B	Class C
Total points	5–6	7–9	10–15
Factor	1 Point	2 Points	3 Points
Total bilirubin (µmol/L)	<34	34–50	>50
Serum albumin (g/L)	>35	28–35	<28
Prothrombin time/international	<1.7	1.71–2.30	>2.30

normalized ratio			
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I–II (or suppressed with medication)	Grade III–IV (or refractory)

Table 7: Interferon ineligible
IFN ineligible is defined as one or more of the below: • Intolerance to IFN • Autoimmune hepatitis and other autoimmune disorders • Hypersensitivity to PEG or any of its components • Decompensated hepatic disease • Major uncontrolled depressive illness • A baseline neutrophil count below 1500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL • A history of preexisting cardiac disease

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 7/10/19.

GUIDELINE UPDATE INFORMATION:

01/01/06	New Medical Coverage Guideline.
12/15/06	Reviewed: reformatted, added note regarding MCG for hepatitis C only and combo therapy is therapy of choice, and added HCPCS codes and updated CPT coding. MCG revised to include Medicare Part D as a program exception.
08/15/07	Review and revision to guideline; consisting of reformatting guideline, adding criteria for treating genotypes 1 and 4 hepatitis C beyond 12 weeks, updated internet links and updated references.
11/15/07	Revision of guideline; consisting of changing all references to length of therapy to weeks to be consistent with Position Statement.
07/15/08	Review and revision to guideline; consisting of adding Alferon® N to MCG, adding note stating that Roferon® brand of interferon alfa-2a has been discontinued by the manufacturer, adding genotypes 5 & 6 to the guideline, adding boxed warning under precautions section and updating references and links.
01/01/09	Annual HCPCS coding update: revised descriptor codes J9212, J9213, J9214 and J9215; deleted 90772; added 96372.
08/15/09	Review and revision to guideline; consisting of adding consideration for up to 72 weeks for genotype 1 infection, highlight “notes” in position statement, updating precautions section and references.
09/15/10	Review and revision to guideline; consisting of updating references.
01/15/11	Revision to guideline; consisting of adding ICD-10 codes.
07/13/11	Review and revision to guideline; consisting of addition of treatment post liver transplant and triple combination therapy to the position statement, added definition of responder, partial responder, null responder, HCPCS code update, deleted Roferon A, added drug information for Incivek™ (telaprevir) and Victrelis® (boceprevir).
10/15/11	Updated guideline to add note preferred pegylated interferon product Pegasys, removed Alferon N from the description and coding section, updated coverage to cirrhosis to include

	compensated only, updated to include justification for need of monotherapy, added pediatric use dual therapy, updated the definitions.
08/15/12	Review and revision to guideline; consisting of updated position statement and drug-drug interaction lists to include new data and recommendations regarding the drug-drug interactions with boceprevir and ritonavir boosted HIV therapies, updated the formatting to include all criteria in a table format, added consideration for extended dosing in genotype 2, 3, added definition of compensated liver disease.
02/15/13	Revision to guideline; consisting of updating format in the note for dual therapy. Removed viral titer quantification < 100 IU/ml from boceprevir TW 8.
08/15/13	Review and revision to guideline; consisting of updating the coverage to include HCV recurrence in liver transplant. Updated response guided therapy chart to provide 24 week of therapy results for telaprevir (Incivek™). Minor formatting changes. Updated ICD-9, ICD-10, and Program Exceptions section. Updated sources.
02/01/14	Revision to guideline; consisting of updating the position statement to include HCV therapy with simeprevir and sofosbuvir and updated the Response Guided Therapy for Table 1 and Therapy by Genotype Table 2. Updated introduction, product information and references.
02/15/14	Revision to guideline; consisting of updating position statement due to updated ASSLD guidelines in the treatment of Hepatitis C infection.
08/15/14	Review and revision to guideline; consisting of description, position statement, dosage/administration, precautions/warning, references.
10/15/14	Revision to guideline; consisting of position statement, dosage/administration, precautions/warnings, references, description.
11/15/14	Revision to guideline; consisting of position statement.
12/15/14	Revision to guideline; consisting of position statement, dosage/administration, coding, other.
02/15/15	Revision to guideline; consisting of position statement, dosage/administration, precautions/warnings, references.
04/01/15	Revisin to guideline; consisting of position statement, dosage/administration, precautions/warnings
06/15/15	Revision to guideline; consisting of position statement
08/15/15	Review and revision to guidelines; consisting of precautions, program exceptions, references
09/15/15	Revision to guideline; consisting of updating position statement, dosage/administration, precautions, coding, and references.
11/01/15	Revision: ICD-9 Codes deleted.
12/18/15	Revision to guideline; consisting of updating position statement and dosage/administration.
03/15/16	Revision to guideline; consisting of updating position statement and dosage/administration, precautions/warnings, references.
08/15/16	Review and revision to guideline; consisting of updating position statement and dosage/administration, precautions/warnings, references.
09/16/16	Revision of guideline to update position statement, dosage/administration, precautions/warnings, references.
11/15/16	Revision to guideline; consisting of updating Tabe 2 with “PEG-IFN + RBV”.
02/15/17	Revision to guideline; consisting of updating position statement, precautions, coding.
8/15/17	Review and revision to guideline consisting of updating position statement and references.
09/15/17	Revision to guideline to include Vosevi in position statement, dosing and administration, references.
11/15/17	Revision to guideline to include Mayvret in position statement, dosing and administration, references.

08/15/18	Revision to guideline to update position statement, references.
11/15/18	Revision to guideline to update position statement
8/15/19	Revision to guideline to update references.