Pharmacy Prior Authorization
Hepatitis C – Clinical Guideline

Viekira Pak/ XR®(ombitasvir, paritaprevir, ritonavir, dasubavir)
Technivie®(ombitasvir, paritaprevir, ritonavir)
Olysio ® (simeprevir)
Epclusa® (sofosbuvir/velpatasvir)
Vosevi™ (sofosbuvir, velpatasvir, voxilaprevir)
Zepatier™ (elbasvir/grazoprevir)
Harvoni® (sofosbuvir/ledipasvir)
Sovaldi® (sofosbuvir)
Daklinza™ (daclatasvir)
Mavyret™ (glecaprevir/pibrentasvir)

Preferred Medication: Mavyret

Note: Ribasphere is preferred and does not require a PA if a Hep C agent is approved

General Authorization Criteria:
For members who meet all of the following (with submitted charts notes and lab results): 18 years of age or older

- Diagnosis of Chronic Hepatitis C for genotype 1, 2, 3, 4, 5, and 6
- Prescribed by a physician specializing in infectious disease, HIV, gastroenterology, hepatology, or transplant
- Documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment when history of abuse is present.
- Baseline HCV-RNA within the last 3 months
- Monitoring treatment plan which includes the following:
    - Provider agrees to submit HCV-RNA at treatment week 4 and 12 weeks post treatment
    - Provider asserts member is ready for treatment and understands treatment regimen and agrees to remain compliant and adherent during the full course of therapy
    - The prescriber must certify that the treatment will be discontinued if the viral load is detectable at week four of treatment and has increased by greater than 10-fold (>1 log10 IU/mL) on repeat testing at week six
- Member has been screened for Hepatitis B (within the previous year) and HBV status addressed appropriately:
    - HBV negative: If not previously vaccinated, vaccination has been initiated or there is a plan to initiate (if not contraindicated)
    - HBV positive/history of HBV positive: Will place on suppressive therapy or monitor for reactivations as is appropriate

Additional Drug Specific Criteria:
Mavyret is the preferred HCV agent documentation will need to be provided to support the medical necessity of non-preferred agents.

Mavyret™ (glecaprevir, pibrentasvir)
Member must meet the following:

- Member is **treatment naïve** and diagnosed with genotype 1, 2, 3, 4, 5, or 6 and meets one of the following:
    - Does not have cirrhosis; maximum duration of treatment is 8 weeks
    - With compensated cirrhosis (Child-Pugh A); maximum duration of treatment is 12 weeks

OR

- Member is **treatment experienced** and meets one of the following:
  - Genotype 1, member previously treated with an ***NS5A inhibitor*** (i.e., Harvoni, Daklinza) and not an NS3/4A inhibitor and does not have cirrhosis or with compensated cirrhosis (child-pugh A); maximum duration of treatment 16 weeks
  - Genotype 1, member previously treated with an **NS3/4A inhibitor** (i.e., Sov/Olysio, Olysio, Incivek, or Victrelis) and not an NS5A inhibitor and does not have cirrhosis or with compensated cirrhosis (Child-pugh A); maximum duration of treatment 12 weeks
  - Genotype 1,2,4,5, or 6 member was previously treated with an a **PRS** containing regimen (i.e., Peg/rbv ±Sov, sov/rbv) and one of the following:
    - Does not have cirrhosis; maximum duration of treatment 8 weeks
    - With compensated cirrhosis (child-pugh A); maximum duration of treatment 12 weeks
  - Genotype 3, member was previously treated with an a **PRS** containing regimen (i.e., Peg/rbv ±Sov, sov/rbv) and does not have cirrhosis or with compensated cirrhosis (child-pugh A); maximum duration of treatment 16 weeks
  - Does not have severe liver impairment Child-Pugh C
  - Will not be in used in combination with rifampin or atazanavir

*PRS (Peg/RBV and Sofosubuvir)

Treatment Naïve (TN):

Genotype	Patient Population	Treatment	Duration of treatment
1,2,3,4,5,6	TN and No Cirrhosis	Mavyret	8 weeks
	TN with compensated cirrhosis (Child-Pugh A)		12 weeks

Treatment Experienced (TE):

Genotype	Patient Population	Treatment	Duration of treatment
1	TE with an NS5A inhibitor[1] without an NS3/4A protease inhibitor (PI) No cirrhosis or with compensated cirrhosis (Child-Pugh A)		16 weeks

	TE with an NS3/4A PI[2] without an NS5A inhibitor No cirrhosis or with compensated cirrhosis (Child-Pugh A)	Mavyret	12 weeks
1,2,4,5,or 6	TE with PRS[3] No cirrhosis		8 weeks
	TE with PRS[3] with compensated cirrhosis (Child-Pugh A)		12 weeks
3	TE with PRS [3] no cirrhosis or with compensated cirrhosis (Child-Pugh A)		16 weeks

1. In clinical trials, subjects were treated with prior regimens containing ledipasvir and sofosbuvir or daclatasvir with pegylated interferon and ribavirin.
2. In clinical trials, subjects were treated with prior regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with pegylated interferon and ribavirin.
3.PRS=Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor.

Epclusa (sofosbuvir/velpatasvir)

Sofosbuvir/velpatasvir

- NS5A RAS testing is required for genotype 3-infected, treatment-experienced patients (with or without cirrhosis) and treatment-naive patients with cirrhosis being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin should be added.

Member must meet the following:

- For genotypes 1, 2, 3,4, 5, or 6 with decompensated cirrhosis, Epclusa will be used in combination with ribavirin the maximum duration of treatment is 12 weeks
- For genotypes 1, 2, 3,4, 5, or 6 without cirrhosis or compensated cirrhosis (Child-Pugh A), the maximum duration of treatment is 12 weeks
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John's Wort, tipranavir/ritonavir)
- Does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

Genotype	Patient Population	Treatment	Duration of treatment

1, 2, 3, 4, 5 or 6	TN and TE (Peg/RBV ± NS3 PI) without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
1, 2, 3, 4, 5 or 6	TN and TE (Peg/RBV ± NS3 PI) With decompensated cirrhosis (Child-Pugh B or C)	Epclusa + RBV	12 weeks

Vosevi ® (sofosbuvir, velpatasvir, voxilaprevir)
Member must meet the following without cirrhosis or compensated cirrhosis (Child-Pugh A):

- Genotype 1, 2, 3, 4,5, or 6, previously treated with an NS5A inhibitor (i.e., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir) OR
- Genotype 1a or 3, previously treated with sofosbuvir without an NS5A inhibitor and with or without (i.e., peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A PI (boceprevir, simeprevir or telaprevir
- Will not exceed the maximum duration of treatment of 12 weeks
- Will not be in used in combination with rifampin
- Does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

Genotype	Patient Population No cirrhosis or with compensated cirrhosis (child-pugh A)	Treatment	Duration of treatment
1, 2, 3, 4, 5, 6	TE with an NS5A inhibitor[a]	Vosevi	12 weeks
1a or 3	TE with Sofosbuvir without an NS5A inhibitor[b]		12 weeks

a. In clinical trials, prior NS5A inhibitor experience included daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir.
b. In clinical trials, prior treatment experience included sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCVNS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir).

Notes: 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.

Zepatier (elbasvir/grazoprevir) HCV or HIV coinfection for genotypes 1 and 4
Member must meet the following:

- For genotype 1a testing is required for NS5A Resistance Associated Variant (RAV); polymorphisms at position 28, 30, 31 or 93, requires a maximum duration of treatment of 16 weeks
- Patient does not have decompensated cirrhosis (Child Pugh B or C)
- Will not be in used in combination with the following medications (i.e., carbamazepine, phenytoin, rifampin, St. John's Wort, cyclosporine, efavirenz, or HIV Protease Inhibitors)

Genotype	Patient Population	Treatment	Duration of treatment

1a	TN or TE (with PegIFN/RBV) Without baseline NS5A† polymorphism	Zepatier	12 weeks
	TN or TE with baseline NS5A polymorphism	Zepatier + RBV	16 weeks
1b	TN or TE (with PegIFN/RBV)	Zepatier	12 weeks
1a§ or 1b	TE (with PegIFN/RBV and PI‡)	Zepatier + RBV	12 weeks *Patients with gt1a (+)NS5A RAV's will require 16 weeks of treatment
4	TN	Zepatier	12 weeks
	TE (with PegIFN/RBV)	Zepatier + RBV	16 weeks

TN=Treatment Naïve, TE=Treatment Experienced
‡Peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor
§The optimal ZEPATIER-based treatment regimen and duration of therapy for PegIFN/RBV/PI-experienced genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31 and 93 has not been established.
†NS5A polymorphism at positions 28, 30, 31 or 93

Harvoni (ledipasvir/sofosbuvir)

Member is 12 years of age or older weighing at least 35 kg and meets the following:

- For genotypes 1, 4, 5, or 6
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John's Wort, tipranavir/ritonavir)
- Member does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

Genotype	Patient Population	Treatment	Duration of treatment
1	TN without cirrhosis (with pretreatment HCV RNA < 6 million IU/ml)	Harvoni	8 weeks
	TN without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks
	TE** without cirrhosis	Harvoni	12 weeks
	TE** with compensated cirrhosis (Child-Pugh A)	Harvoni	24 weeks or

		Harvoni+ RBV	12 weeks (If eligible for RBV)
	TN and TE with decompensated cirrhosis (Child-Pugh B or C)	Harvoni + RBV	12 weeks
	TN or TE** without or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks
1 or 4	TN and TE liver transplant recipients without t cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni + RBV	12 weeks
4, 5, or 6	TN and TE** without or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks

** TE with Peg/RBV ± PI

Children (12 years of age and older or weighing at least 35 kg)

Genotype	Patient Population	Treatment	Duration of treatment
1	TN without or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks
	TE without cirrhosis	Harvoni	12 weeks
	TE with compensated cirrhosis (Child-Pugh A)	Harvoni	24 weeks
4, 5 or 6	TN or TE without or with compensated cirrhosis (Child-Pugh A)	Harvoni	12 weeks

Sovaldi (sofosbuvir) in combination with ribavirin
Patient must meet the following:

- Hepatocellular Carcinoma (awaiting transplantation)
  - Not previously transplanted AND
  - Must meet Milan criteria (defined as the presence of tumor 5 cm or less in diameter in patients with single hepatocellular carcinomas and no more than 3 tumor nodules, each 3 cm or less in diameter in patients with multiple tumors and no extra hepatic manifestations or evidence of vascular invasions of tumor)
  - Maximum duration of treatment 48 weeks
- Will not be in used in combination with the following medications (i.e., amiodarone, carbamazepine, oxcarbazepine, phenytoin, rifampin, St. John's Wort, tipranavir/ritonavir)
- Member does not have eGFR < 30 ml/min or has ESRD requiring hemodialysis

All other regimens not listed above will be considered on case by case bases

Non-Coverage Criteria:

- Coverage for greater than the duration of treatment outlined in the tables within the guideline
- Lost or stolen medication or fraudulent use

- Lifetime expectancy for less than 12 months due to non-liver related comorbid conditions
- Viekira, Viekira XR, Technivie, and Zepatier in member's with Child Pugh B or C
- Olysio, Daklinza and Sovaldi used as monotherapy
- Use in combination with other DAA's unless indicated
- Any contraindications to any of the agents

Initial Authorization :

Approve for the full course of therapy

Additional Information:

Hep B Reactivation:

Per AASLD: All patients initiating HCV DAA therapy should be assessed for HBV coinfection with testing for HBsAg, anti-HBs, and anti-HBc. HBV vaccination is recommended for all susceptible individuals.

Ribavirin dosing recommendations and key contraindications:

- The daily dosage of ribavirin is weight-based (1000 mg for patients <75 kg and 1200 mg for those ≥75 kg) administered orally in two divided doses with food
- For patients with decompensated cirrhosis or post-transplantation the recommended starting dose is 600mg once daily up to 1000 mg as tolerated
- Ribavirin is contraindicated in women who are pregnant or may become pregnant, including in men whose female partners are pregnant
- Ribavirin is contraindicated in patients with hemoglobinopathies (i.e., sickle cell anemia or thalassemia)

HIV and HCV Drug interactions/links:

http://www.hcvguidelines.org/full-report/unique-patient-populations-patients-hivhcv-coinfection

http://www.hep-druginteractions.org/

https://www.hcvguidelines.org/evaluate/resistance

Case Management: For plans that support HCV the following will be required:

- Member and prescriber agree to participate with nursing and pharmacy case management of the plan to assure member compliance with the prescribed medication, access to services, lab tests, lab reviews and offer medical guidance as needed to optimize a successful outcome for the member.

Response Definitions:

- **Partial Responder:** Member experiences at least a 2-log10 (100 times) drop in HCV RNA, but has the inability to fully remove the virus from the blood by end of treatment.
- **Null/Non Responder:** Member does not experience at least 2-log10 (100 times) drop in HCV RNA 8-12 weeks of treatment.

- **Relapse:** Member has an undetectable HCV viral load at end of treatment regimen, but who has a detectable viral load within 12-24 weeks after stopping treatment.

References:

1. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Recommendations for Testing, Managing, and Treating Hepatitis C. http://www.hcvguidelines.org/full-report-view. Accessed Sept 2016.
2. Harvoni [Prescribing Information]. Foster City, CA: Gilead Sciences, Inc.; Apr 2017
3. Sovaldi™ [Prescribing Information]. Foster City, CA: Gilead Sciences, Inc.; Apr 2017
4. Viekira PAK [Prescribing Information]. North Chicago, Ill: AbbVie, Inc.; Mar 2017
5. Olysio [Prescribing Information]. Titusville, NJ: Jansen.; Feb 2017
6. Daklinza [Prescribing Information]. Princeton, NJ: Brystol-Meyers Squibb; Feb 2017Technivie [Prescribing Information]. North Chicago, Ill: AbbVie, Inc.; Mar 2017
7. Zepatier [Prescribing Information]. Whitehouse Station, NJ: Merck, Inc.: Feb 2017
8. Epclusa [Prescribing Information]. Foster City, CA: Gilead Sciences, Inc.; Aug 2017
9. Viekira XR [Prescribing Information]. North Chicago, Ill: AbbVie, Inc.; Mar 2017
10. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Recommendations for Testing, Managing, and Treating Hepatitis C. http://www.hcvguidelines.org/full-report-view. Accessed July 6 2016
11. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Recommendations for Testing, Managing, and Treating Hepatitis C. http://www.hcvguidelines.org/full-report-view. Accessed Sept 2016. http://www.hcvguidelines.org/evaluate/monitoring; accessed July 10,2017
12. Vosevi [Prescribing Information]. Foster City, CA: Gilead Sciences, Inc.; Jul 2017
13. Mavyret [Prescribing Information]. North Chicago, Ill: AbbVie, Inc.; Aug 2017
14. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed Sept 28, 2017.
15. Annals of Internal Medicine Vol 161 No 7 December 2017 pp794-805.