Aetna Better Health®

Pharmacy Prior Authorization
Hepatitis C – Clinical Guideline

Preferred Medications:
Mavyret™ (glecaprevir/pibrentasvir), sofosbuvir/velpatasvir

Nonpreferred Medications:
Viekira Pak® (ombitasvir, paritaprevir, ritonavir, dasubavir), Zepatier™ (elbasvir/grazoprevir), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), Epclusa® (sofosbuvir/velpatasvir), Vosevi™ (sofosbuvir, velpatasvir, voxilaprevir)

Note: ribavirin 200 mg capsule and 200 mg tablet are preferred and do not require a Prior Authorization if a Hepatitis C agent is approved

Note: ledipasvir and sofosbuvir (Harvoni) will be authorized for children 3 through 5 years of age (documentation will be required to support medical necessity of inability to utilize the authorized generic formulation)

General Authorization Criteria:

- **Member meets all the following criteria** (Along with submitted documentation of charts notes and lab results):
  - Diagnosis is Chronic Hepatitis C for genotype 1, 2, 3, 4, 5, and 6
  - Prescribed by, or in consultation with a physician specializing in infectious disease, gastroenterology, hepatology, or transplant
  - Fibrosis score (Note: Fibrosis score F0-F4 is eligible for treatment)
  - Baseline hepatitis C virus ribonucleic acid (HCV-RNA) within the last 3 months
    - If newly diagnosed with Hepatitis C infection within the past year, 2 Hepatitis C Virus Ribonucleic Acid (HCV-RNA) levels must be taken at least 6 months apart to demonstrate a chronic Hepatitis C Virus infection.
  - Prescriber counseling regarding risks of alcohol or intravenous drug abuse, and an offer of referral for substance use disorder treatment when history of abuse is present.
  - Monitoring treatment plan which includes the following:
    - Provider agrees to monitor hepatitis C virus ribonucleic acid (HCV-RNA) at treatment week 4- and 12-weeks post treatment
    - Provider asserts member is ready for treatment, understands treatment regimen, and agrees to remain compliant, and adherent during the full course of therapy
  - Member has been screened for Hepatitis B virus (HBV) within previous year, and Hepatitis B virus (HBV) status is addressed appropriately:
    - Hepatitis B Virus (HBV) negative: If not previously vaccinated, vaccination has been initiated, or there is a plan to initiate (if not contraindicated)
    - Hepatitis B Virus (HBV) positive/history of Hepatitis B Virus (HBV) positive: Will place on suppressive therapy, or monitor for reactivations as is appropriate

Direct-Acting Antiviral Therapy Retreatment

(Requests for repeat direct-acting antiviral therapy will be considered on a case by case basis):

- All the following additional criteria will apply:
  - Current infection has been present for greater than or equal to 6 months
  - Prescriber must answer all the following questions:
    - Is retreatment necessary due to treatment failure or reinfection?
    - Was member adherent (for example, few to no missed doses) with previous direct-acting antiviral therapy? If not, why?
    - Were there any additional factors that led to direct-acting antiviral therapy treatment failure? If so, describe these factors, and how they have been addressed, or are no longer relevant.
  - Member must be evaluated for alcohol, and substance abuse using a validated screening tool
  - For recent history (within the past 6 months) of alcohol, or substance abuse, the following criteria is required:
    - Documentation member completed, or is participating in recovery program, receiving alcohol, or substance abuse counseling services, or seeing an addiction specialist as part of Hepatitis C Virus treatment
    - Documentation member is not actively participating in illicit substance use, or alcohol abuse with confirmatory laboratory testing such as urine drug screen
  - Prescriber attests to all the following:
    - Member is willing and able to comply with requirements of proposed retreatment plan
    - Any factors that may have led to nonadherence with previous treatment(s) have been addressed
    - Member has received education regarding risk behaviors (for example, intravenous drug use) associated with Hepatitis C Virus infection).

Non-Coverage Criteria:

- Coverage for greater than duration of treatment outlined in tables within the guideline
- Lost or stolen medication or fraudulent use
- Lifetime expectancy of less than 12 months, due to non-liver related comorbid conditions
- Viekira Pak, Mavyret and Zepatier in members with Child-Pugh B or C
- Use in combination with other direct-acting antivirals (DAAs) unless indicated
- Any contraindications to any of the agents

Additional Criteria:

Member meets the following:

- Mavyret
  - Age is 12 years or older, and weight is greater than or equal to 45 kilograms
  - There is no severe liver impairment Child-Pugh C
  - Will not be in used in combination with potent P-Gp/CYP3A inducer drug (St. John's wart, phenytoin, rifampin or, carbamazepine, efavirenz,) or atazanavir, ritonavir, tipranavir, etc.
- sofosbuvir/velpatasvir
  - Age is 6 years or older, and weight is greater than or equal to 17 kilograms

- Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C) in combination with ribavirin for a duration of 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)
- Baseline NS5A resistance-associated substitutions (RAS) testing for HCV genotype 3-infected, treatment-naive patients with cirrhosis and treatment-experienced patients (with or without cirrhosis).

Mavyret™ (glecaprevir/pibrentasvir)

Treatment Naïve:

Genotype	Member Population	Treatment	Duration of treatment
1,2,3,4,5,6	Treatment Naïve without cirrhosis	Mavyret	8 weeks
	Treatment Naïve with compensated cirrhosis (Child-Pugh A)		8 weeks

Treatment Experienced:

Genotype	Member Population	Treatment	Duration of treatment
1	Treatment Experienced with a Non-Structural Protein 5A (NS5A) inhibitor[1] without a Non-Structural Protein S3/4A (NS3/4A) protease inhibitor No cirrhosis or compensated cirrhosis (Child-Pugh A)	Mavyret	16 weeks
	Treatment Experienced with a NS3/4A Protease Inhibitor[2] without a Non-Structural Protein 5A (NS5A) inhibitor No cirrhosis or compensated cirrhosis (Child-Pugh A)		12 weeks
	Treatment Experienced with peginterferon/ribavirin/sofosbuvir[3] No cirrhosis		8 weeks

1, 2, 4, 5, or 6	Treatment Experienced with peginterferon/ribavirin/sofosbuvir[3] Compensated cirrhosis (Child-Pugh A)		12 weeks
3	Treatment Experienced with peginterferon/ribavirin/sofosbuvir[3] No cirrhosis or compensated cirrhosis (Child-Pugh A)		16 weeks

Liver or Kidney Transplant Recipients:

Genotype	Member Population	Treatment	Duration of Treatment
1, 2, 3, 4, 5 or 6	Treatment naïve and treatment experienced	Mavyret	12 weeks
1	Treatment experienced with a Non-Structural Protein 5A (NS5A) inhibitor without prior treatment with a Non-Structural Protein S3/4A (NS3/4A) protease inhibitor		16 weeks
3	Treatment experienced with regimens containing interferon, ribavirin, and/or sofosbuvir only		

sofosbuvir/velpatasvir:

Genotype	Patient Population	Treatment	Duration of treatment
1, 2, 3, 4, 5 or 6	Treatment Naïve and Treatment Experienced (Peg/RBV ± NS3 protease inhibitor (PI)) without cirrhosis or with	Sofosbuvir/velpatasvir	12 weeks

	compensated cirrhosis (Child-Pugh A)		
1, 2, 3, 4, 5 or 6	Treatment Naïve and Treatment Experienced (Peg/RBV ± NS3 protease inhibitor (PI)) With decompensated cirrhosis (Child-Pugh B or C)		

Initial Authorization:

- Approve for the full course of therapy
- All request must be sent to Medical Director for final determination

Additional Information:

INTERNAL USE ONLY NOTE:

For non-preferred agents the following website may be utilized to aid and in review:
https://www.hcvguidelines.org/

INTERNAL USE ONLY NOTE:

Drug interactions associated with estrogen containing oral contraceptives or statins does not clinically justify to NOT using preferred agent Mavyret. See table

Drug	Effect on conc ion	Clinical Comments
Ethinyl estradiol containing medications (combined oral contraceptives)	↔ glecaprevir ↔ pibrentasvir	Coadministration of MAVYRET may increase the risk of ALT elevations
Atorvastatin Lovastatin Simvastatin	↑ atorvastatin ↑ lovastatin ↑ simvastatin	Coadministration may increase the concentration. Increased statin concentrations may increase the risk of myopathy. Coadministration with these statins is not recommended.
Pravastatin	Pravastatin ↑	Coadministration may increase the concentration Increased statin concentrations may increase the risk of myopathy. Reduce pravastatin dose by 50% when co-administered with MAVYRET.
Rosuvastatin	↑ rosuvastatin	Coadministration may increase the concentration. Increased statin concentrations may increase the risk of myopathy. Administered with MAVYRET at a dose that does not exceed 10 mg.
Fluvastatin pitavastatin	↑ Fluvastatin pitavastatin	Coadministration may increase the concentrations and may increase the risk of myopathy, Use the lowest approved dose. If higher doses are needed, use the lowest necessary statin dose based on a risk/benefit assessment.

Hepatitis B Reactivation: Per the American Association for the Study of Liver Disease (AASLD): All members initiating hepatitis C virus (HCV) direct-acting antivirals (DAA) therapy should be assessed for hepatitis B virus (HBV) coinfection with testing for hepatitis B surface antigen (HBsAg), hepatitis B surface

antibody (anti-HBs), and hepatitis B core antibodies (anti-HBc). HBV vaccination is recommended for all susceptible individuals.

Ribavirin dosing recommendations and key contraindications:

- Daily dosage of ribavirin is weight-based (1000 mg for members less than 75 kg and 1200 mg for those greater than or equal to 75 kg), administered orally in two divided doses with food
- For members with decompensated cirrhosis with post-transplantation, recommended starting dose is 600mg/day (in two divided doses), increased monthly by 200mg to a weight-based dosing of 1200mg/day for members more than 75kg and 1000mg/day, for members 75kg or less in two divided doses with food
- Ribavirin is contraindicated in women who are pregnant or may become pregnant, including in men whose female partners are pregnant
- Ribavirin is contraindicated in members with hemoglobinopathies (for example, sickle-cell anemia or thalassemia)

HIV and Hepatitis C virus (HCV) Drug interactions/links:

- https://www.hcvguidelines.org/unique-populations/hiv-hcv
- http://www.hep-druginteractions.org/
- https://www.hcvguidelines.org/evaluate/resistance

Case Management:

- For plans that support hepatitis C virus the following will be required:
  - Member and prescriber agree to participate with nursing, and pharmacy case management of the plan, to assure compliance with prescribed medication, access to services, lab tests, lab reviews and offer medical guidance as needed to optimize successful outcome.

Response Definitions:

- **Partial Responder:**
  - Member experiences at least a 2-log10 (100 times) drop in hepatitis C virus ribonucleic acid (HCV-RNA) but is unable to fully remove the virus from blood by end of treatment.
- **Null/Non-Responder:**
  - Member does not experience at least 2-log10 (100 times) drop in hepatitis C virus ribonucleic acid (HCV-RNA) 8-12 weeks of treatment.
- **Relapse:**
  - Member has undetectable hepatitis C virus viral load at end of treatment regimen but has detectable viral load within 12-24 weeks after stopping treatment.

Cirrhosis and Fibrosis Definitions:

- **Fibrosis:**
  - Histological consequence (activation of hepatic stellate cells) of wound-healing process, which results in net imbalance of collagen fiber synthesis and decomposition
- **Cirrhosis:**

- Always developed from fibrosis, cirrhosis is an advanced stage of liver fibrosis with distortion in hepatic vasculature (for example portal hypertension) and structure (for example, abnormal lobules)
  - Compensated: Varices present
  - Decompensated: Development of ascites, variceal hemorrhage, encephalopathy, and/or jaundice

	Metavir	Fibrosis
Non-Cirrhosis Stage of Chronic Liver Disease	F0	No fibrosis
	F1	Portal fibrosis without septa
	F2	Septal fibrosis (portal-portal)
	F3	Septal fibrosis (portal-central
Cirrhotic Stage of Chronic Liver Disease	F4	Compensated cirrhosis
		Decompensated cirrhosis

References:

1. Epclusa ® [package insert]. Gilead Sciences, Inc., Foster City, CA; March 2020. https://www.gilead.com/-/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf. Accessed March 23, 2020.
2. Harvoni ® [package insert]. Gilead Sciences, Inc., Foster City, CA; March 2020. https://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf. Accessed March 23, 2020.
3. "Hepatitis C Guidance 2019 Update: American Association for the Study of Liver Diseases–Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection." Hepatology, vol. 71, no. 2, 2020, pp. 686–721., doi:10.1002/hep.31060.
4. Mavyret ™ [package insert]. AbbVie Inc., North Chicago, IL; January 2020. https://www.rxabbvie.com/pdf/mavyret_pi.pdfAccessed March 23, 2020.
5. Sovaldi ® [package insert]. Gilead Sciences, Inc., Foster City, CA; March 2020. https://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf. Accessed March 23, 2019.
6. Suk, K. T. (2015). Staging of liver fibrosis or cirrhosis: The role of hepatic venous pressure gradient measurement. World Journal of Hepatology,7(3), 607. doi:10.4254/wjh.v7.i3.607
7. Viekira Pak ® [package insert]. AbbVie Inc., North Chicago, IL; December 2019. https://www.rxabbvie.com/pdf/iekirapak_pi.pdf Accessed March 23, 2020.
8. Vosevi ™ [package insert]. Gilead Sciences, Inc., Foster City, CA; November 2019. http://www.gilead.com/~/media/files/pdfs/medicines/liver-disease/vosevi/vosevi_pi.pdf. Accessed March 23, 2020.
9. Zepatier ™ [package insert]. Merck & Co., Inc., Whitehouse Station, NJ; December 2019. https://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdfAccessed March 23, 2020.