

Clinical Criteria for Hepatitis C (HCV) Therapy

Pre-Treatment Evaluation

- Must have chronic hepatitis C and HCV genotype and sub-genotype documented;
- Patients who have prior exposure to DAA therapy must have a pre-DAA genotype and post-DAA genotype documented (Appendix B);
- HCV RNA quantitative within 90 days of application for therapy;
- Liver biopsy or other accepted test (Appendix A) demonstrating liver fibrosis corresponding to Metavir score of greater than or equal to 1(one), unless the patient is less than 21 years old **or** has a viral condition which is known (documented) to result in an accelerated hepatic disease (fibrosis) progression and /or hepatic decompensation than what is normally expected from the course of chronic HCV;
- Previous HCV treatment history and outcome;
- HIV status and, if HIV positive, current antiretroviral regimen and degree of viral suppression within 6 months of application for therapy;
- HBV status and, if active HBV disease, current antiretroviral regimen and degree of viral suppression within 6 months of application for therapy;
- Adherence evaluation: Providers must assess and document the patient's ability to adhere to therapy;
- Drug resistance testing as indicated; and

Patient Treatment Plan

- It is required that the patient have a treatment plan developed by, or in collaboration with, a provider with expertise in Hepatitis C management. [Sample treatment plan documents are available for use.](#)
- If the patient or their partner is of childbearing age, at least two (2) forms of contraception must be used (by the patient or their partner) if a RBV-containing regimen is prescribed throughout the duration of therapy and for six (6) months after the regimen is completed.

Drug Therapy

- Must be in accordance with FDA approved indications.

Treatment Options¹:

Genotype 1a:

○ **Elbasvir/grazoprevir (Zepatier™)²**

- Prior to requesting/initiating therapy with this agent, genotype testing for baseline NS5A polymorphisms is REQUIRED, in order to determine treatment length.
- Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment	Treatment length
Treatment naïve, without baseline NS5A polymorphisms	Zepatier	12 weeks
Treatment naïve, with baseline NS5A polymorphisms	Zepatier + weight based ribavirin	16 weeks
Treatment experienced (PegIFN/RBV), without baseline NS5A polymorphisms	Zepatier	12 weeks
Treatment experienced (PegIFN/RBV), with baseline NS5A polymorphisms	Zepatier + weight based ribavirin	16 weeks

○ **Glecaprevir/pibrentasvir (Mavyret™)⁶**

- Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

○ **Ledipasvir/sofosbuvir (Harvoni®)³**

- Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis*	12 weeks
Treatment naïve, with cirrhosis	12 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis**	24 weeks

*8 weeks of treatment can be considered in treatment naive patients without cirrhosis who have pretreatment HCV RNA levels less than 6 million IU/mL.

**A 12 week regimen with weight-based ribavirin may be considered.

- **Sofosbuvir/velpatasvir (Epclusa®)**⁴
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**⁵
 - Prior DAA experience with an NS5A inhibitor or sofosbuvir
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Genotype 1b:

- **Elbasvir/grazoprevir (Zepatier™)**²
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve	12 weeks
Treatment experienced (PegIFN/RBV)	12 weeks

- **Glecaprevir/pibrentasvir (Mavyret™)**⁶
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

○ **Ledipasvir/sofosbuvir (Harvoni®)**³

- Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis*	12 weeks
Treatment naïve, with cirrhosis	12 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis**	24 weeks

*8 weeks of treatment can be considered in treatment naïve patients without cirrhosis who have pretreatment HCV RNA levels less than 6 million IU/mL.

**A 12 week regimen with weight-based ribavirin may be considered.

○ **Sofosbuvir/velpatasvir (Epclusa®)**⁴

- Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

○ **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**⁵

- Prior DAA experience with an NS5A inhibitor
- Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
- Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Genotype 2:

○ **Glecaprevir/pibrentasvir (Mavyret™)**⁶

- Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)**⁴

- Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**⁵

- Prior DAA experience with an NS5A inhibitor
- Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval

Genotype 3:

- **Glecaprevir/pibrentasvir (Mavyret™)**⁶

- Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	16 weeks
Treatment experienced, with compensated cirrhosis	16 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)**⁴

- Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)⁵**
 - Prior DAA experience with an NS5A inhibitor or sofosbuvir
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Genotype 4:

- **Elbasvir/grazoprevir (Zepatier™)²**
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment	Treatment length
Treatment naïve	Zepatier	12 weeks
Treatment experienced (PegIFN/RBV)	Zepatier + weight based ribavirin	16 weeks

- **Glecaprevir/pibrentasvir (Mavyret™)⁶**
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Ledipasvir/sofosbuvir (Harvoni®)³**
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, with or without cirrhosis	12 weeks
Treatment experienced, with or without cirrhosis	12 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)**⁴
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**⁵
 - Prior DAA experience with an NS5A inhibitor
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Genotype 5 and 6:

- **Glecaprevir/pibrentasvir (Mavyret™)**⁶
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Ledipasvir/sofosbuvir (Harvoni®)**³
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR \geq 30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, with or without cirrhosis	12 weeks
Treatment experienced, with or without cirrhosis	12 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)**⁴
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**⁵
 - Prior DAA experience with an NS5A inhibitor
 - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
 - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

References:

1. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. March 13, 2019 accessed.
2. Zepatier [package insert]. Whitehouse Station, NJ: Merck and Co., Inc., January 2016.
3. Harvoni [package insert]. Foster City, CA: Gilead Sciences, Inc., November 2015.
4. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc., June 2016.
5. Vosevi [package insert]. Foster City, CA: Gilead Sciences, Inc., August 2017.
6. Mavyret [package insert]. North Chicago, IL: AbbVie Inc., August 2017.

Appendix A: Acceptable tests for determination of fibrosis in HCV

Noninvasive methods for determination of liver disease

Numerous noninvasive methodologies have been developed to determine the degree of fibrosis in patients infected with chronic HCV. These methodologies employ either the use of biomarkers or evaluation of liver stiffness to make a determination regarding the degree of liver fibrosis.¹ Below is a table of acceptable noninvasive testing and the score which is equivalent to metavir stage F1 as available.

Noninvasive test	Score equivalent to metavir stage F1
FibroScan (transient elastography)*	7.1 kPa ²
Point shear wave elastography (pSWE) Acoustic radiation force impulse imaging (AFRI)*	1.34 m/s ³
MR elastography	3.45 kPa ⁴
Fibrosure®	0.27

*Ultrasound testing is not able to be used to differentiate between F0 and F1 disease and a blood test will be required for treatment approval

1. Castera L. Noninvasive methods to assess liver disease in patients with hepatitis B or C. *Gastroenterology* 2012;142:1293-1302.
2. Foucher J, Chanteloup E, Vergniol J, et al. Diagnosis of cirrhosis by transient elastography (Fibroscan): a prospective study. *Gut* 2006;55:403-8.
3. Ferraioli G, Tinelli C, Dal Bello B, et al. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study. *Hepatology* 2012;56:2125.
4. Singh S, Venkatesh SK, Wang Z, et al. Diagnostic performance of magnetic resonance elastography in staging liver fibrosis: a systematic review and meta-analysis of individual participant data. *Clin Gastroenterol Hepatol* 2015;13:440.

Appendix B: HCV Treatment Definitions

Retreatment: Previous exposure to an HCV treatment direct acting antiviral (DAA) regimen, which does NOT result in achievement of SVR and current need for an additional course of therapy to treat chronic HCV infection.

Conditions required:

- Detectable HCV RNA at 12 weeks post treatment.
- HCV genotype is the SAME before and after the INITIAL HCV treatment regimen.

Reinfection: Exposure to an HCV treatment regimen, which results in achievement of SVR.

Conditions required:

- Detectable HCV RNA > 12 weeks post treatment
- HCV genotype is DIFFERENT after the INITIAL HCV treatment regimen.
- Current infection has been present \geq 6 months.