Clinical Criteria for Hepatitis C (HCV) Therapy

CLINICAL DOCUMENTATION REQUIREMENTS*:

A. Completed PA form
B. Recent (within the last six (6) months) provider note, unless the patient is cirrhotic then the last provider note must be within 90 days of prior authorization request
C. Genotype
D. HCV RNA (up to and including 180 days of application for therapy), unless the patient is cirrhotic then the baseline lab values must be within 90 days of prior authorization request
E. Baseline lab values
    i. Total bilirubin (only in cirrhotic patient)
    ii. Albumin (only in cirrhotic patient)
    iii. INR (only in cirrhotic patient)
F. Fibrosis score
G. HIV viral load (ONLY if the patient is co-infected) within six (6) months of application for therapy
H. HBV viral load (ONLY if the patient has active infection) within six (6) months of application for therapy

*B-H: Actual documentation required as opposed to attestations or values on the PA Form

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 A);
- HCV RNA quantitative within 180 days of application for therapy, unless the patient is cirrhotic then the baseline lab values must be within 90 days of prior authorization request;
- Liver biopsy or other accepted fibrosis test (ex. fibrosure, hepascore/fibroscore, fibroscan, point shear wave elastography (PSWE) acoustic radiation force impulse imaging (AFRI)**;
- 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.

**Not required in the treatment of HCV-Uninfected Recipients of Non-liver Organs from HCV-Viremic Donors

Patient Treatment Plan

- It is recommended that the patient have a treatment plan developed by the treating clinician. 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
- RBV= Ribavirin, IFN = Interferon, CTP = Child-Turcotte-Pugh

Preferred Agents	Non-Preferred Agents
• Sofosbuvir/Velpatasvir (authorized generic for Epclusa®) • Glecaprevir/pibrentasvir (Mavyret®)	• Elbasvir/Grazoprevir (Zepatier®) • Sofosbuvir/Velpatasvir (brand Epclusa®) • Ledipasvir/Sofosbuvir Tablet (Harvoni® and authorized generic for Harvoni®) • Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®)

- **Elbasvir/grazoprevir (Zepatier™)**

I. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to authorized generic Epclusa (sofosbuvir/velpatasvir) OR Mavyret, unless one of the following conditions apply:

A. Individual is using in **one** of the following antiviral treatment regimens (Label/AASLD/IDSA 2019):

1. As monotherapy for **one** of the following:

a. Individual is treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b, or Genotype 1a without a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and Y93; **AND**
b. Individual meets one of the following criteria:
    i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
    ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

c. Individual is treatment-naïve, with compensated[1] cirrhosis or without cirrhosis, and Genotype 4; **OR**
d. Individual is a dual P/R[2b] treatment-experienced virologic relapser, with compensated[1] cirrhosis or without cirrhosis, and Genotype 4;
AND
e. Individual meets one of the following criteria:
    i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
    ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

f. Individual is post-kidney transplantation, treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b, or Genotype 1a without a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and/or Y93, or Genotype 4; **AND**
g. Individual meets one of the following criteria:
    i. Prior trial of Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
    ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

2. In combination with ribavirin for **one** of the following:
   a. Individual is treatment-naïve, dual P/R[2b], or triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1a with a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and/or Y93; **OR**
   b. Individual is triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b or 1a without a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and Y93;

   AND

   c. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
      ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

   OR

   d. Individual is a dual P/R[2b]treatment-experienced with prior on-treatment virologic failure, with compensated[1] cirrhosis or without cirrhosis, and Genotype 4; **AND**
   e. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
      ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

   OR

   f. In combination with sofosbuvir for dual P/R[2b] treatment-experienced individuals, with compensated cirrhosis[1], and Genotype 3; **AND**
   g. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier or sofosbuvir; **OR**
      ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**

iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**

iv. Individual has had a prior trial of Mavyret with documented hypersensivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier or sofosbuvir, AND is not a candidate for the Epclusa regimen when it contains ribavirin, due to being ribavirin ineligible (examples include individuals with hemoglobinopathies, significant cardiac disease, creatinine clearance less than 50 mL/min, documented severe allergic reaction, or pregnancy).

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

- **Ledipasvir/sofosbuvir (Harvoni® and authorized generic Harvoni®)**

I. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to authorized generic Epclusa (sofosbuvir/velpatasvir) OR Mavyret, unless one of the following conditions apply:

A. Individual is using in **one** of the following antiviral treatment regimens (Label, AASLD/IDSA 2019):

1. Individual is 3 years of age or older; **AND**
2. As monotherapy for **one** of the following:
   a. Individual is treatment-naïve with compensated[1] cirrhosis or without cirrhosis and Genotype 1; **OR**
   b. Individual is dual P/R[2b] or triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis and Genotype1;

   AND

   c. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
      ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
      iv. Individual is 3 to 5 years of age;

OR

d. Individual is treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis and Genotype 4, 5 or 6; **AND**
e. Individual meets one of the following criteria:
    i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
    ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
    iv. Individual is 3 to 5 years of age;

OR

f. Individual is triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis and Genotype 4, 5 or 6; **AND**
g. Individual meets one of the following criteria:
    i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
    ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
    iv. Individual is 3 to 5 years of age;

OR

h. Individual is treatment-naïve or treatment-experienced without a sofosbuvir or NS5A[2a]-containing regimen, ribavirin ineligible, with decompensated[1] cirrhosis and Genotypes 1, 4, 5 or 6; **AND**
i. Individual meets one of the following criteria:
    i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**

ii. Individual is currently on and completing a course of therapy with the
iii. requested regimen; **OR** Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
iv. Individual is 3 to 17 years of age.

OR

j. Individual is a post-kidney transplant recipient, treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotypes 1, 4, 5, or 6; **AND**
k. Individual meets one of the following criteria:
   i. Prior trial of Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
   ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
   iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
   iv. Individual is 3 to 11 years of age;

OR

l. Individual is a post-liver allograft transplant recipient, treatment naïve or experienced, without cirrhosis[b], and Genotype 1, 4, 5, or 6; **AND**
m. Individual meets one of the following criteria:
   i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
   ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
   iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
   iv. Individual is 3 to 11 years of age;

OR

3. Individual is 3 years of age or older; **AND**

4. In combination with ribavirin for **one** of the following:
   a. Individual is sofosbuvir (non simeprevir-containing) treatment-experienced without cirrhosis and Genotype 1 **(except Genotype 1b)**; **AND**
   b. Individual meets one of the following criteria:
      i. Prior trial of Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
      ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
      iv. Individual is 3 to 11 years of age;

OR

   c. Individual is sofosbuvir (non simeprevir-containing) treatment-experienced without cirrhosis and Genotype 1b; **AND**
   d. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
      ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
      iv. Individual is 3 to 11 years of age;

OR

   e. Individual is dual P/R[2b] or triple[2d] treatment-experienced with compensated[1] cirrhosis, and Genotype 1; **OR**
   f. Individual is dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis, and Genotype 4; **AND**
   g. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**
      ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted

with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**

iv. Individual is 3 to 5 years of age

OR

h. Individual is treatment-naïve, or treatment-experienced with decompensated[1] cirrhosis and Genotypes 1, 4, 5 or 6; **AND**

i. Individual meets one of the following criteria:

i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; OR

ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**

iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**

iv. Individual is 3 to 5 years of age

OR

j. Individual is a post-liver allograft transplant recipient, with compensated[1] cirrhosis, or without cirrhosis, and Genotypes 1, 4, 5 or 6; **AND**

k. Individual meets one of the following criteria:

i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**

ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**

iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**

iv. Individual is 3 to 11 years of age;

OR

l. Individual is a post-liver allograft transplant recipient, decompensated[1] cirrhosis, and Genotypes 1, 4, 5 or 6; **AND**

m. Individual meets one of the following criteria:

i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Harvoni; **OR**

ii. Individual is currently on and completing a course of therapy with the requested regimen; **OR**

iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
iv. Individual is 3 to 17 years of age.

AND

II. If requesting Harvoni 45 mg/200 mg oral pellets, individual is unable to swallow the oral tablet dose form due to a clinical condition, including, but not limited to the following:
A. Dysphagia; **OR**
B. Individual's age.

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

Requests for brand Epclusa (sofosbuvir/velpatasvir) may be approved if the prior authorization criteria are met; **AND**

I. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to authorized generic Epclusa (sofosbuvir/velpatasvir).

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

I. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to authorized generic Epclusa (sofosbuvir/velpatasvir) OR Mavyret, unless one of the following conditions apply:

A. Individual is using in **one** of the following antiviral treatment regimens (Label, AASLD/IDSA 2019):
1. As monotherapy for **one** of the following:
a. Individual is NS5A[2a] treatment-experienced with compensated[1] cirrhosis or without cirrhosis, and Genotype 1 or 2;

OR
b. Individual is treatment experienced with a sofosbuvir-containing regimen without an NS5A[2b] inhibitor, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1a; **AND**
c. Individual meets one of the following criteria:
i. Prior trial of Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi; **OR**
ii. Individual is currently on and completing a course of therapy with Vosevi; **OR**
iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

d. Individual is treatment experienced with a sofosbuvir-containing regimen without an NS5A[2b] inhibitor, with compensated[1] cirrhosis or without cirrhosis, and Genotype 3;

OR

e. Individual is dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis, and Genotype 3; **AND**
f. Individual meets one of the following criteria:
    i. Prior trial of Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi; **OR**
    ii. Individual is currently on and completing a course of therapy with Vosevi; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

g. Individual is treatment-naïve, with compensated[1] cirrhosis, polymorphism present at the Y93H amino acid position, and Genotype 3; **AND**
h. Individual meets one of the following criteria:
    i. Prior trial of generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi; **OR**
    ii. Individual has a documented hypersensitivity to Mavyret, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi AND individual is not a candidate for the Epclusa regimen due to being ribavirin ineligible (examples include individuals with hemoglobinopathies, significant cardiac disease, creatinine clearance less than 50 mL/min, documented severe allergic reaction, or pregnancy); **OR**
    iii. Individual is currently on and completing a course of therapy with Vosevi; **OR**
    iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

i. Individual is dual P/R[2b] treatment-experienced without cirrhosis, polymorphism present at the Y93H amino acid position, and Genotype 3; **AND**

j. Individual meets one of the following criteria:

i. Prior trial of generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi; **OR**

ii. Individual has a documented hypersensitivity to Mavyret, as manifested by a severe allergic reaction to any ingredient which is not also in Vosevi, AND individual is not a candidate for the Epclusa regimen due to being ribavirin ineligible (examples include individuals with hemoglobinopathies, significant cardiac disease, creatinine clearance less than 50 mL/min, documented severe allergic reaction, or pregnancy); **OR**

iii. Individual is currently on and completing a course of therapy with Vosevi; **OR**

iv. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

k. Individual is DAA[2e] treatment-experienced with compensated[1] cirrhosis or without cirrhosis, and Genotype 3, 4, 5 or 6;

OR

B. In combination with ribavirin for the following (AASLD/IDSA 2019):

1. Individual is NS5A[2a] treatment-experienced, with compensated[1] cirrhosis and Genotype 3;

OR

2. Individual had treatment failure with Mayvret (glecaprevir/pibrentasvir) monotherapy, with compensated cirrhosis and Genotype 1, 2, 3, 4, 5, or 6.

Treatment Naïve Patients			
Genotype	**No Cirrhosis**	**Compensated Cirrhosis**	**Decompensated Cirrhosis (CTP B or C)**
1a	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 8 wks* Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks (if no NS5A RAS)	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks (if no NS5A RAS)	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
1a	***Alternative Regimens*** Zepatier + RBV x 16 (if NS5A RAS present)	***Alternative Regimens*** Zepatier + RBV x 16 (if NS5A RAS present)	***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks
1b	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 8 wks* Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
1b			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks
2	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks
2			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks
3	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks (if no Y93 RAS) Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks
3		***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks (if Y93 RAS present)	***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks
4	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
4			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks
5 or 6	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
5 or 6			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks

*if HCV RNA < 6 million

Treatment Experienced Patients arrange by treatment			
Genotype	**No Cirrhosis**	**Compensated Cirrhosis**	**Decompensated Cirrhosis (CTP B or C)**
IFN + RBV Experienced			
1a	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks (if no NS5A RAS)	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks (if no NS5A RAS)	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBV x 12 wks
1a	***Alternative Regimens*** Zepatier (elbasvir/grazoprevir) + RBV x 16 (if NS5A RAS present)	***Alternative Regimens*** Harvoni (ledipasvir/sofosbuvir) + RBV x 12 wks Zepatier (elbasvir/grazoprevir) + RBV x 16 (if NS5A RAS present)	***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks
1b	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
1b		***Alternative Regimens*** Harvoni (ledipasvir/sofosbuvir) + RBV x 12 wks	***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks
2	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks
2			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks
3	Epclusa (sofosbuvir/velpatasvir) x 12 wks (if no Y93 RAS) Mavyret (glecaprevir/pibrentasvir) x 16 wks	Mavyret (glecaprevir/pibrentasvir) x 16 wks	*No currently FDA approved treatment regimens*
3	***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks (if Y93 RAS present)	***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks	
4	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks Zepatier (elbasvir/grazoprevir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks Zepatier (elbasvir/grazoprevir) x 12 wks	*No currently FDA approved treatment regimens*
4		***Alternative Regimens*** Harvoni ledipasvir/sofosbuvir) + RBV x 12 wks	
5 or 6	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	*No currently FDA approved treatment regimens*
NS3 PI Experienced			
1a or 1b	Epclusa (sofosbuvir/velpatasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks

	Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks	Mavyret (glecaprevir/pibrentasvir) x 8 wks	Harvoni (ledipasvir/sofosbuvir) + RBV x 12 wks
1a or 1b			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks Harvoni (ledipasvir/sofosbuvir) x 24 wks
SOF Experienced and NS5A Naïve			
2	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x12 wks	*No currently FDA approved treatment regimens*
NS5A Experienced			
1a or 1b	Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	*No currently FDA approved treatment regimens*
1a or 1b	***Alternative Regimens*** Mavyret (glecaprevir/pibrentasvir) x 16 wks	***Alternative Regimens*** Mavyret (glecaprevir/pibrentasvir) x 16 wks	
2	Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	*No currently FDA approved treatment regimens*
DAA Experienced			
3	Mavyret (glecaprevir/pibrentasvir) x 16 wks Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	Mavyret (glecaprevir/pibrentasvir) x 16 wks Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	*No currently FDA approved treatment regimens*
4,5 or 6	Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	Vosevi (sofosbuvir/velpatasvir/voxilaprevir) x 12 wks	*No currently FDA approved treatment regimens*

Post Liver and Kidney Transplant Patients			
Genotype	**No Cirrhosis**	**Compensated Cirrhosis**	**Decompensated Cirrhosis (CTP B or C)**
1	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
1			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks* Harvoni (ledipasvir/sofosbuvir) x 24 wks*
2	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks
2			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks*
3	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks
3			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks*
4	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
4			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks* Harvoni (ledipasvir/sofosbuvir) x 24 wks*
5 or 6	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 12 wks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks Harvoni (ledipasvir/sofosbuvir) + RBVx 12 wks
5 or 6			***Alternative Regimens*** Epclusa (sofosbuvir/velpatasvir) x 24 wks* Harvoni (ledipasvir/sofosbuvir) x 24 wks*

*24 week duration should be used in treatment experienced patients

Treatment of HCV-Uninfected Recipients of Non-liver Organs from HCV-Viremic Donors	
Genotype	**No need to evaluate for cirrhosis**
1, 2, 3, 4, 5, 6	Epclusa (sofosbuvir/velpatasvir) x 12 weeks Mavyret (glecaprevir/pibrentasvir) x 8 weeks

Pediatric Patients Treatment Naïve or IFN Experienced	
Genotype	**No Cirrhosis or Compensated Cirrhosis**
1	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks
2	Epclusa (sofosbuvir/velpatasvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks
3	Mavyret (glecaprevir/pibrentasvir) x 8 wks
4,5 or 6	Epclusa (sofosbuvir/velpatasvir) x 12 wks Harvoni (ledipasvir/sofosbuvir) x 12 wks Mavyret (glecaprevir/pibrentasvir) x 8 wks

Pediatric Dosing				
Epclusa (sofosbuvir/velpatasir) For patients ≥ 6 years old OR at least 17 kg		**Harvoni (ledipasavir/sofobuvir) For patients ≥ 3 years old**		**Mavyret (glecaprevir/pibrentasvir) For patients ≥ 12 years old OR at least 45 kg**
Body Weight	Once Daily Dose	Body Weight	Once Daily Dose	
17 kg to < 30 kg	200 mg/ 50 mg	< 17 kg	33.75 mg/ 150 mg	
≥ 30 kg	400 mg/ 100 mg	17 kg to < 35 kg	45 mg/ 200 mg	
		≥ 35 kg	90 mg/ 400 mg	

No Genotype Determined or Multiple Genotypes	
No cirrhosis or Compensated Cirrhosis	**Decompensated Cirrhosis (CTP B or C)**
Epclusa (sofosbuvir/velpatasvir) x 12 weeks Mavyret (glecaprevir/pibrentasvir) x 8 weeks	Epclusa (sofosbuvir/velpatasvir) + RBV x 12 wks
	Alternative Regimens Epclusa (sofosbuvir/velpatasvir) x 24 wks

Notes:

1. **Compensated Liver Disease**:
   According to the American Association for the Study of Liver Diseases (AASLD/IDSA 2017), the specific criteria for compensated liver disease include all of the following: a total bilirubin; serum albumin; prothrombin time/INR; presence of ascites; and presence of hepatic encephalopathy. However, these criteria do not establish a comprehensive definition of compensated liver disease. The AASLD guidance refers to compensated liver disease as Class A based on the Child Pugh-Turcotte (CPT) classification scoring system.

   Moderate to Severe (Decompensated) Liver Disease:
   The AASLD guidance refers to decompensated (moderate to severe) liver disease as Class B or C based on the Child-Pugh Turcotte (CPT) classification scoring system.

Child Pugh Classification (AASLD/IDSA 2017)

Parameters			
Points Assigned	1 point	2 points	3 points
Total Bilirubin (µmol/L)	<34	34-50	>50
Serum Albumin (g/L)	>35	28-35	<28
Prothrombin time/INR	<1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic Encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

Child Pugh Score Interpretation (AASLD/IDSA 2017)

Class A	5-6 points	Well compensated liver disease
Class B	7-9 points	Significant functional compromise (moderate hepatic impairment)
Class C	10-15 points	Uncompensated liver disease (severe hepatic impairment)

2. Past Treatment Exposure Definitions (AASLD/IDSA 2017):
   a. NS5A Inhibitor: includes daclatasvir, ledipasvir, elbasvir, ombitasvir, pibrentasvir, or velpatasvir-containing regimens

b. P/R: includes peginterferon (or non-pegylated interferon) ± ribavirin
c. NS3/4A Protease Inhibitor: includes simeprevir, grazoprevir, paritaprevir, glecaprevir, and voxilaprevir-containing regimens
d. Triple therapy: includes NS3 protease inhibitor (simeprevir, boceprevir or telaprevir) plus peginterferon and ribavirin
e. Direct Acting Antiviral (DAA): includes NS5A inhibitors, NS3/4A protease inhibitors, and NS5B polymerase inhibitors (sofosbuvir, dasabuvir)

3. Chronic Kidney Disease (CKD) Definitions (AASLD/IDSA 2017):
Severe CKD (Stage 4): eGFR 15-29 mL/min
End-Stage CKD (Stage 5): eGFR < 15 mL/min

4. **Metavir Scoring Systems for Fibrosis Staging (AASLD 2009):**

Stage (F)	
0	No fibrosis
1	Periportal fibrotic expansion
2	Periportal septae 1 (septum)
3	Porto-central septae
4	Cirrhosis

5. Hepatitis C virus (HCV) direct acting antiviral (DAA) agents have a black box warning for risk of hepatitis B virus (HBV) reactivation in individuals with HCV-HBV co-infection. Individuals should be tested for evidence of current or prior HBV infection prior to initiation of DAA therapy. HBV reactivation has been reported in HCV/HBV co-infected individuals currently taking or previously completed DAA therapy and not concomitantly receiving HBV antiviral therapy. Some cases of HBV reactivation have led to fulminant hepatitis, hepatic failure, and death. Individuals should be monitored for hepatitis flare or HBV reactivation during and following HCV DAA therapy. Individuals should be appropriately managed for HBV infection as indicated.

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Appendix A: 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 ≥ six (6) months