Hepatitis C Medications
Effective 05/01/2022

Plan	☐ MassHealth ☒ MH UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit (NLX)		
Specialty Limitations	These medications have been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Specialty Medications**		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	N/A		

Overview:

For MassHealth members:
GENERIC Harvoni™ (ledipasvir/sofosbuvir 90mg/400mg) is a preferred combination agent HCV medication for Genotype 1, 4, 5 or 6
GENERIC Epclusa® (sofosbuvir/velpatasvir) is a preferred combination agent HCV medication for *GENOTYPES 1-6*
Mavyret™ is a preferred combination agent HCV medication for Genotypes 1-6
Current prior authorizations will be grandfathered for the life of the prior authorization
****NOTE: Generic Harvoni (ledipasvir/sofosbuvir) is available and is preferred for all MassHealth members =/>18 years of age. BRAND NAME Harvoni may be dispensed to members ages 3 to < 18 ONLY per Mass Health.**

No PA	Drugs that require PA
HCV protease inhibitor/HCV NS5A inhibitor	
	Mavyret® (glecaprevir/pibrentasvir)[PD]
HCV NS5A inhibitor/HCV NS5B polymerase inhibitor	
	Harvoni® (ledipasvir/sofosbuvir)†‡
HCV NS5B polymerase inhibitor/HCV NS5A inhibitor	
	Epclusa® (sofosbuvir/velpatasvir)†‡
HCV NS5B polymerase inhibitor/HCV NS5A inhibitor/HCV protease inhibitor	
	Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)
HCV NS5A inhibitor/HCV protease inhibitor	
	Zepatier® (elbasvir/grazoprevir)

[PD] Preferred Drug. In general, a trial of the preferred drug or clinical rationale for prescribing a non-preferred drug within a therapeutic class.
†Authorized generic available. Both brand and authorized generic require a PA.
‡ Preferred Drug. In general, a trial of the preferred drug or clinical rationale for prescribing a non-preferred drug within a therapeutic class. Please note: the generic formulation is preferred.

AllWays Health Partners will continue to review non-preferred products on a case by case basis and cover when medically necessary.

Coverage Guidelines

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners who are currently receiving treatment with the requested medication (e.g. genotype, combination therapy, dose, treatment duration, etc.) for chronic hepatitis C infection, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization may be granted for members when ALL the following criteria are met, and documentation is provided:

Epclusa® (sofosbuvir/velpatasvir)†
Treatment-naïve members with or without compensated cirrhosis (Child Turcotte Pugh [CTP] class A)*
Prescriber provides documentation of **ALL** of the following:
1. Member is ≥3 years of age
2. Requested regimen does not have drug-drug interactions with member's concomitant medications
3. Requested quantity is ≤ 1 unit/day
4. If the request is for BRAND NAME Epclusa®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

**Requests can be approved for 12 weeks*

Treatment-experienced† members with or without compensated cirrhosis (Child Turcotte Pugh [CTP] class A)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥ 3 years of age
4. Appropriate dosing
5. Requested duration is 12 weeks
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
    a. For children < 8 years old – See Appendix
7. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
    a. For children < 8 years old – See Appendix
8. For members ≥ 18 years old with genotype 3 only, **ONE** of the following:
    a. Absence of cirrhosis and **ONE** of the following
        i. Testing results document absence of NS5A resistance-associated substitution Y93H

ii. Testing results document presence of NS5A resistance-associated substitution Y93H and requested regimen includes ribavirin

b. Compensated cirrhosis and requested regimen includes ribavirin

9. Requested regimen does not have drug-drug interactions with member's concomitant medications
10. If the request is for BRAND NAME Epclusa®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

†*Treatment-experienced members are those who have failed treatment with peginterferon alfa and ribavirin (with or without protease inhibitor).*

Harvoni® (ledipasvir/sofosbuvir)†

Treatment-naïve members without cirrhosis

Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C
2. Genotype 1
3. Member is ≥ 3 years of age
4. Appropriate dosing
5. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
6. Stage of liver disease is early stage (e.g. Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3) *Children <8 years old – See Appendix*
7. **ONE** of the following:
    a. Member is ≥3 and <18 years old and requested duration is 12 weeks
    b. Member is ≥18 years of age **AND ONE** of the following:
        i. Baseline viral load (within the last six months) < 6 million IU/mL and requested duration is eight weeks*
        ii. **BOTH** of the following:
            a) Baseline viral load (within the last six months) ≥ 6 million IU/mL and requested duration is 12 weeks*
            b) Clinical rationale for use instead of sofosbuvir/velpatasvir
8. Requested regimen does not have drug-drug interactions with member's concomitant medications
9. If the request is for BRAND NAME Harvoni®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

Treatment-naïve members with compensated cirrhosis (Child Turcotte Pugh [CTP] class A) **OR** *Treatment-experienced† members without cirrhosis*

Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C
2. Genotype 1
3. **ONE** of the following:
    a. Member is ≥18 years of age and clinical rationale for use instead of sofosbuvir/velpatasvir
    b. Member is ≥3 and <18 years of age
4. Appropriate dosing
5. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*

6. Stage of liver disease is early stage (e.g. Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis) *Children <8 years old – See Appendix*
7. Requested duration is 12 weeks
8. Requested regimen does not have drug-drug interactions with member's concomitant medications
9. If the request is for BRAND NAME Harvoni®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

Treatment-experienced† *members with compensated cirrhosis* (Child Turcotte Pugh [CTP] class A)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C
2. Genotype 1
3. **ONE** of the following:
    a. Member is ≥18 years of age and clinical rationale for use instead of sofosbuvir/velpatasvir
    b. Member is ≥3 and <18 years of age
4. Appropriate dosing
5. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
6. **ONE** of the following:
    a. Member is ≥3 and <18 years of age and requested duration is 24 weeks
    b. Member is ≥18 years of age **AND BOTH** of the following:
        i. Requested regimen includes ribavirin
        ii. Requested duration is 12 weeks
    c. Member is ≥18 years of age **AND BOTH** of the following:
        i. Requested duration is 24 weeks
        ii. Clinical rationale for use instead of 12-week treatment with ledipasvir/sofosbuvir and ribavirin§
7. Requested regimen does not have drug-drug interactions with member's concomitant medications
8. If the request is for BRAND NAME Harvoni®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

**Requests for 12 weeks that provide clinical rationale for use instead of sofosbuvir/velpatasvir while also documenting that member has HIV-coinfection (anywhere on PA or medical records) can be approved even if viral load is <6 million (if all other criteria are met). Requests for 8 weeks for members with HIV-coinfection, s/p liver or kidney transplant, or decompensated cirrhosis should be denied-LOI due to lack of studies supporting this treatment duration in these populations.*
†Treatment-experienced members are those who have failed treatment with an interferon with or without (ribavirin and/or protease inhibitor).
§Required regimen that includes ribavirin may be bypassed if prescriber documents recent anemia i.e., hemoglobin (Hgb) <12 g/dL (male) ***OR*** *<11 g/dL (females) as a clinical rationale. Prior intolerance or anemia with ribavirin may be considered on a case-by-case basis – Consult clinical reviewer, if needed.*

Treatment-naïve or treatment-experienced members without cirrhosis or with compensated cirrhosis* (Child Turcotte Pugh [CTP] class A)

Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 4, 5, or 6
3. **ONE** of the following:
    a. Member is ≥ 18 years of age and clinical rationale for use instead of sofosbuvir/velpatasvir
    b. Member is ≥ 3 and < 18 years of age
4. Appropriate dosing
5. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
6. Stage of liver disease is early stage (e.g. Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis) *Children <8 years old – See Appendix*
7. Requested duration is 12 weeks†
8. Requested regimen does not have drug-drug interactions with member's concomitant medications
9. If the request is for BRAND NAME Harvoni®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

**Treatment-experienced members are those who have failed treatment with an interferon with or without (ribavirin and/or protease inhibitor).*

†*Requests for 8 weeks can be approved in members age ≥18 years of age with genotype 4 (except genotype 4r) who are treatment-naïve without cirrhosis with baseline viral load (within the last six months) <6 million IU/mL.*

Mavyret® (glecaprevir/pibrentasvir)

Treatment-naïve members with or without compensated cirrhosis (Child Turcotte Pugh [CTP] class A)

Prescriber provides documentation of **ALL** of the following*:
1. Member is ≥3 years of age
2. Requested regimen does not have drug-drug interactions with member's concomitant medications
3. For tablets, requested quantity is ≤ 3 unit/day
4. For packets of pellets, requested quantity is ≤ 5 unit/day

Treatment-experienced (failed treatment with interferon, peginterferon, ribavirin only; sofosbuvir plus peginterferon and ribavirin only; or sofosbuvir plus ribavirin only) members with or without compensated cirrhosis (Child Turcotte Pugh [CTP] class A)

Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥ 3 years of age
4. Requested dose is three 100 mg/40 mg tablets once daily
5. For genotype 1, 2, 4, 5, or 6, **ONE** of the following:
    a. Absence of cirrhosis and requested duration is eight weeks‡
    b. Compensated cirrhosis and requested duration is 12 weeks
6. For genotype 3, requested duration is 16 weeks
7. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
8. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
9. Requested regimen does not have drug-drug interactions with member's concomitant medications

Treatment-experienced (failed treatment with an HCV NS5A inhibitor without an HCV protease inhibitor) *members with or without compensated cirrhosis (Child Turcotte Pugh [CTP] class A)*
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1
3. Member is ≥3 years of age*
4. Requested dose is three 100 mg/40 mg tablets once daily
5. Requested duration is 16 weeks
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
7. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
8. Requested regimen does not have drug-drug interactions with member's concomitant medications

**Requests can be approved for 8 weeks (or 12 weeks if treatment-naïve with cirrhosis and HIV-coinfection)*
[†]Requests for 12 weeks for members with prior sofosbuvir failure (as the only DAA) and absence of cirrhosis – Consult clinical reviewer.

Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)
Treatment-experienced (failed treatment with an HCV NS5A inhibitor)* *members with or without compensated cirrhosis* (Child Turcotte Pugh [CTP] class A)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥18 years of age
4. Requested dose is 400 mg/100 mg/100 mg once daily
5. For members with genotype 3 and compensated cirrhosis, requested regimen includes ribavirin
6. Requested duration is 12 weeks
7. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
8. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
9. Requested regimen does not have drug-drug interactions with member's concomitant medications

Treatment-experienced (failed treatment with sofosbuvir[‡] without an HCV NS5A inhibitor) members with or without compensated cirrhosis (Child Turcotte Pugh [CTP] class A)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1a or 3[§]
3. Member is ≥18 years of age
4. Requested dose is 400 mg/100 mg/100 mg once daily
5. Requested duration is 12 weeks
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
7. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
8. Requested regimen does not have drug-drug interactions with member's concomitant medications

**In clinical trials, prior NS5A inhibitors included daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir. Requests noting prior Mavyret® or Vosevi® failure - see Appendix IV.*
‡In clinical trials, prior sofosbuvir-containing regimens included peginterferon alfa/ribavirin, ribavirin, and HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
§Requests for members with genotype 1b, 2, 4, 5, or 6 who have failed sofosbuvir-containing regimen(s) without HCV NS5A inhibitor can be evaluated using criteria above.
Requests for members with genotype 3 who are treatment-experienced (peginterferon alfa/ribavirin only) with compensated cirrhosis should provide clinical rationale for use instead of Mavyret® for 16 weeks and sofosbuvir/velpatasvir plus ribavirin for 12 weeks.

Zepatier® (elbasvir/grazoprevir)
Treatment-naïve or treatment-experienced members (failed treatment with peginterferon alfa and ribavirin only)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1
3. Contraindication to **ALL** combination products FDA-approved for the treatment of HCV genotype 1 infection (e.g., ledipasvir/sofosbuvir, Mavyret®, sofosbuvir/velpatasvir)*
4. Member is ≥18 years of age
5. Requested dose is 50 mg/100 mg once daily
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
7. Stage of liver disease is early stage (e.g. Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
8. Member does not have decompensated cirrhosis (Child Turcotte Pugh Class B or C)
9. **ONE** of the following:
    a. Request is for genotype 1a and **BOTH** of the following:
        i. Testing results document absence of NS5A resistance-associated substitutions at amino acid positions 28, 30, 31, and 93
        ii. Requested duration is 12 weeks
    b. Request is for genotype 1a and **BOTH** of the following:
        i. Testing results document presence of NS5A resistance-associated substitutions at amino acid positions 28, 30, 31, or 93
        ii. Requested regimen includes ribavirin† and requested duration is 16 weeks
    c. Request is for genotype 1b and requested duration is 12 weeks
10. Requested regimen does not have drug-drug interactions with member's concomitant medications

Treatment-experienced members (failed treatment with an HCV protease inhibitor plus peginterferon alfa and ribavirin only)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1
3. Contraindication to **ALL** combination products FDA-approved for the treatment of HCV genotype 1 infection (e.g., ledipasvir/sofosbuvir, Mavyret®, sofosbuvir/velpatasvir)*
4. Member is ≥18 years of age
5. Requested dose is 50 mg/100 mg once daily
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)

7. Stage of liver disease is early stage (e.g. Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
8. Member does not have decompensated cirrhosis (Child Turcotte Pugh Class B or C)
9. Requested regimen includes ribavirin
10. **ONE** of the following:
    a. Request is for genotype 1a and **BOTH** of the following:
        i. Testing results document absence of NS5A resistance-associated substitutions at amino acid positions 28, 30, 31, and 93
        ii. Requested duration is 12 weeks
    b. Request is for genotype 1a and **BOTH** of the following:
        i. Testing results document presence of NS5A resistance-associated substitutions at amino acid positions 28, 30, 31, or 93
        ii. Requested duration is 16 weeks
    c. Request is for genotype 1b and requested duration is 12 weeks
11. Requested regimen does not have drug-drug interactions with member's concomitant medications

Treatment-naïve or treatment-experienced members (failed treatment with peginterferon alfa and ribavirin only)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 4
3. Contraindication to **ALL** combination products FDA-approved for the treatment of HCV genotype 4 infection (e.g., ledipasvir/sofosbuvir, Mavyret®, sofosbuvir/velpatasvir)*
4. Member is ≥ 18 years of age
5. Requested dose is 50 mg/100 mg once daily
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
7. Stage of liver disease is early stage (e.g. Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
8. Member does not have decompensated cirrhosis (Child Turcotte Pugh Class B or C)
9. **ONE** of the following:
    a. Member is treatment-naïve or has a history of relapse to prior peginterferon and ribavirin treatment and requested duration is 12 weeks
    b. Member has a history of on-treatment virologic failure (failure to suppress or breakthrough) while on peginterferon and ribavirin treatment **AND BOTH** of the following:
        i. Requested regimen includes ribavirin
        ii. Requested duration is 16 weeks
10. Requested regimen does not have drug-drug interactions with member's concomitant medications

Continuation Criteria:
Reauthorization requires physician documentation of continuation of therapy and will be reviewed on a cases by case basis.

†Authorized generic available. Both brand and authorized generic require a PA.

Appendix:
Appendix A: Drug-Interactions

Epclusa® (sofosbuvir/velpatasvir)
Sofosbuvir/velpatasvir may be safely coadministered with any of the following drugs/combinations:

- Edurant® (rilpivirine)
- Emtriva® (emtricitabine)
- Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide)
- Isentress® (raltegravir)
- Prezista® (darunavir) with ritonavir
- Reyataz® (atazanavir) with ritonavir
- Tivicay® (dolutegravir)

Drug Interactions (Not All Inclusive)

<table>
<tr><th>Concomitant Drug Class: Drug Name</th><th>Effect on Concentration</th><th>Recommendations</th></tr>
<tr><td>H2-receptor antagonists:
e.g., famotidine</td><td>↓ velpatasvir</td><td>H2-receptor antagonist doses greater than famotidine 40 mg twice daily (or equivalent H2-receptor antagonist) may decrease ledipasvir concentration.
<table>
<tr><th>H2 antagonist</th><th>Comparable dose</th></tr>
<tr><td>Tagamet® (cimetidine)</td><td>400 mg to 800 mg twice daily</td></tr>
<tr><td>Pepcid® (famotidine)</td><td>40 mg twice daily</td></tr>
<tr><td>Axid® (nizatidine)</td><td>300 mg twice daily</td></tr>
<tr><td>Zantac® (ranitidine)</td><td>150 mg four times daily</td></tr>
</table></td></tr>
<tr><td>Proton-pump inhibitors (PPI):
e.g., such as omeprazole</td><td>↓ velpatasvir</td><td>Coadministration of omeprazole or other PPIs is not recommended. If coadministration is medical necessary, administer Epclusa® (sofosbuvir/velpatasvir) with food four hours before omeprazole 20 mg. Use with other PPIs has not been studied.
If use with a PPI at a dose exceeding omeprazole 20 mg/day is requested, PA should address whether discontinuing the PPI or reducing the dose to omeprazole 20 mg once daily (or equivalent) is an option.
<table>
<tr><th>Proton-pump inhibitor</th><th>Comparable dose</th></tr>
<tr><td>Aciphex® (rabeprazole)</td><td>20 mg</td></tr>
<tr><td>Dexilant® (dexlansoprazole)</td><td>30 mg</td></tr>
<tr><td>Nexium® (esomeprazole)</td><td>20 mg</td></tr>
<tr><td>Prevacid® (lansoprazole)</td><td>30 mg</td></tr>
<tr><td>Prilosec® (omeprazole)</td><td>20 mg</td></tr>
<tr><td>Protonix® (pantoprazole)</td><td>40 mg</td></tr>
</table></td></tr>
<tr><td>Antiarrhythmics:
amiodarone</td><td>Unknown</td><td>Coadministration with amiodarone may result in serious bradycardia. Coadministration is not recommended; if</td></tr>
</table>

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
		coadministration is required, cardiac monitoring is recommended.
Antiarrhythmics: digoxin	↑ digoxin	Coadministration with digoxin may increase the concentration of digoxin. Monitor therapeutic concentration of digoxin during coadministration.
Anticancers: topotecan	↑ topotecan	Coadministration is not recommended.
Anticonvulsants: carbamazepine, phenytoin, phenobarbital, oxcarbazepine	↓ sofosbuvir ↓ velpatasvir	Coadministration is not recommended.
Antimycobacterial: rifabutin, rifampin, rifapentine	↓ sofosbuvir ↓ velpatasvir	Coadministration is not recommended.
Efavirenz-containing regimens (Atripla® or Sustiva®)	↓ velpatasvir	Coadministration with efavirenz-containing regimens is not recommended.
Intelence® (etravirine)	Unknown	Coadministration is not recommended by AASLD/IDSA.
Nevirapine	Unknown	Coadministration is not recommended by AASLD/IDSA.
Tenofovir disoproxil fumarate	↑ tenofovir	Avoid Epclusa® (sofosbuvir/velpatasvir) use if CrCl<60 mL/min. This warning does not apply to tenofovir alafenamide e.g., Descovy® (emtricitabine/tenofovir alafenamide), Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) or Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide).
HMG-CoA Reductase Inhibitors: **rosuvastatin**	↑ rosuvastatin	Coadministration may increases risk of myopathy, including rhabdomyolysis. The dose of rosuvastatin should not exceed 10 mg.
St. John's wort	↓ sofosbuvir ↓ velpatasvir	Coadministration is not recommended.
Aptivus® (tipranavir)/ritonavir	↓ sofosbuvir ↓ velpatasvir	Coadministration is not recommended.

Harvoni® (ledipasvir/sofosbuvir)
Ledipasvir/sofosbuvir x 8 weeks has not been specifically studied in patients with HIV-coinfection. *Requests for 8-week treatment duration noting HCV/HIV-coinfection (or history of claims for HIV antiretrovirals in POPS) should be denied.*

Ledipasvir/sofosbuvir may be safely coadministered with any of the following drugs/combinations:

- Atripla® (efavirenz/emtricitabine/tenofovir) as long as CrCl≥60 mL/min
- Complera® (rilpivirine/emtricitabine/tenofovir) as long as CrCl≥60 mL/min
- Descovy® (emtricitabine/tenofovir alafenamide)
- Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide)

- Isentress® (raltegravir)
- Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide)

Drug Interactions (Not All Inclusive)

<table>
<tr><th>Concomitant Drug Class: Drug Name</th><th>Effect on Concentration</th><th>Recommendations</th></tr>
<tr><td>H₂-receptor antagonists:
e.g., famotidine</td><td>↓ ledipasvir</td><td>H₂-receptor antagonist doses greater than famotidine 40 mg twice daily (or equivalent H₂-receptor antagonist) may decrease ledipasvir concentration.
<table>
<tr><th>H₂ antagonist</th><th>Comparable dose</th></tr>
<tr><td>Tagamet® (cimetidine)</td><td>400 mg to 800 mg twice daily</td></tr>
<tr><td>Pepcid® (famotidine)</td><td>40 mg twice daily</td></tr>
<tr><td>Axid® (nizatidine)</td><td>300 mg twice daily</td></tr>
<tr><td>Zantac® (ranitidine)</td><td>150 mg four times daily</td></tr>
</table></td></tr>
<tr><td>Proton-pump inhibitors (PPI):
e.g., omeprazole</td><td>↓ ledipasvir</td><td>PPI doses greater than omeprazole 20 mg daily (or equivalent PPI) may decrease ledipasvir concentration.
<table>
<tr><th>Proton-pump inhibitor</th><th>Comparable dose</th></tr>
<tr><td>Aciphex® (rabeprazole)</td><td>20 mg</td></tr>
<tr><td>Dexilant® (dexlansoprazole)</td><td>30 mg</td></tr>
<tr><td>Nexium® (esomeprazole)</td><td>20 mg</td></tr>
<tr><td>Prevacid® (lansoprazole)</td><td>30 mg</td></tr>
<tr><td>Prilosec® (omeprazole)</td><td>20 mg</td></tr>
<tr><td>Protonix® (pantoprazole)</td><td>40 mg</td></tr>
</table></td></tr>
<tr><td>Antiarrhythmics:
amiodarone</td><td>Unknown</td><td>Coadministration with amiodarone may result in serious bradycardia. Coadministration is not recommended; if coadministration is required, cardiac monitoring is recommended.</td></tr>
<tr><td>Antiarrhythmics:
digoxin</td><td>↑ digoxin</td><td>Coadministration with digoxin may increase the concentration of digoxin. Monitor therapeutic concentration of digoxin during coadministration.</td></tr>
<tr><td>Anticonvulsants:
carbamazepine, phenytoin, phenobarbital, oxcarbazepine</td><td>↓ ledipasvir
↓ sofosbuvir</td><td>Coadministration with carbamazepine, phenytoin, phenobarbital, or oxcarbazepine may decrease the concentration of ledipasvir and sofosbuvir, leading to reduced therapeutic effect of Harvoni® (ledipasvir/sofosbuvir). Coadministration is not recommended.</td></tr>
<tr><td><u>Antimycobacterial:</u>
<u>rifabutin, rifampin, rifapentine</u></td><td>↓ ledipasvir
↓ sofosbuvir</td><td>Coadministration with rifabutin or rifapentine may decrease the concentration of ledipasvir and sofosbuvir, leading to reduced therapeutic effect of Harvoni® (ledipasvir/sofosbuvir). Coadministration is not recommended. Coadministration with rifampin, a P-gp inducer, is not recommended.</td></tr>
<tr><td><u>Tenofovir disoproxil fumarate</u></td><td>↑ tenofovir</td><td>Avoid Harvoni® (ledipasvir/sofosbuvir) use if CrCl<60 mL/min.
Drug interaction is avoided with these alternatives:
Descovy® (emtricitabine/tenofovir alafenamide)</td></tr>
</table>

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
		Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide)
Regimens containing BOTH tenofovir disoproxil fumarate AND an HIV protease inhibitor/ritonavir atazanavir/ritonavir + emtricitabine/tenofovir darunavir/ritonavir + emtricitabine/tenofovir lopinavir/ritonavir + emtricitabine/tenofovir	↑ tenofovir	The safety of increased tenofovir concentrations in the setting of Harvoni® (ledipasvir/sofosbuvir) and a HIV protease inhibitor/ritonavir has not been established. Consider alternative HCV or antiretroviral therapy to avoid increases in tenofovir exposures. If coadministration is necessary, monitor for tenofovir-associated adverse reactions. **Drug interaction is avoided with these alternatives:** Descovy® (emtricitabine/tenofovir alafenamide) Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide)
Stribild® (elvitegravir, cobicistat, emtricitabine, and tenofovir)	↑ tenofovir	The safety of increased tenofovir concentrations in the setting of Harvoni® (ledipasvir/sofosbuvir) and the combination of elvitegravir, cobicistat, emtricitabine and tenofovir has not been established. Coadministration is not recommended. Consider Genvoya® (elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide) as a safe alternative.
HMG-CoA Reductase Inhibitors: **rosuvastatin**	↑ rosuvastatin	Coadministration may increases risk of myopathy, including rhabdomyolysis. Coadministration with rosuvastatin is not recommended.
St. John's wort	↓ ledipasvir ↓ sofosbuvir	Coadministration of Harvoni® (ledipasvir/sofosbuvir) with St. John's wort, a P-gp inducer is not recommended.
Aptivus® (tipranavir)/ritonavir	↓ ledipasvir ↓ sofosbuvir	Coadministration with tipranavir/ritonavir may decrease the concentration of ledipasvir and sofosbuvir, leading to reduced therapeutic effect of Harvoni® (ledipasvir/sofosbuvir). Coadministration is not recommended.

Mavyret® (glecaprevir/pibrentasvir)
Please use the following table **AND** http://www.hep-druginteractions.org/checker to screen for drug interactions.

Mavyret® may be safely coadministered with any of the following drugs/combinations:

- Edurant® (rilpivirine)
- Emtriva® (emtricitabine)
- Epivir® (lamivudine)
- Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide)
- Isentress® (raltegravir)

- Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate)
- Tivicay® (dolutegravir)
- Vemlidy® (tenofovir alafenamide) or Viread® (tenofovir disoproxil fumarate)
- Ziagen® (abacavir)

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
Antiarrhythmics: Digoxin	↑ digoxin	Measure serum digoxin concentrations before initiating glecaprevir/pibrentasvir. Decrease digoxin dose by approximately 50% or by modifying the dosing frequency and continue monitoring.
Anticoagulants: dabigatran etexilate	↑ dabigatran	Modify dabigatran dose per prescribing information in the setting of renal impairment.
Anticonvulsants: carbamazepine, phenytoin, phenobarbital, oxcarbazepine	↓ glecaprevir ↓ pibrentasvir	Coadministration with carbamazepine may lead to reduced antiviral efficacy and is not recommended. Similar interaction is expected with phenytoin, phenobarbital, and oxcarbazepine per http://www.hep-druginteractions.org.
Antimycobacterial: rifampin	↓ glecaprevir ↓ pibrentasvir	Coadministration is contraindicated due to potential loss of antiviral efficacy.
Ethinyl estradiol-containing products: oral contraceptives	-	Coadministration may increase the risk of ALT elevations and is not recommended.
St. John's wort	↓ glecaprevir ↓ pibrentasvir	Coadministration may lead to reduced antiviral efficacy and is not recommended.
Antiretrovirals:		
atazanavir	↑ glecaprevir ↑ pibrentasvir	Coadministration is contraindicated due to increased risk of ALT elevations.
darunavir, lopinavir, ritonavir	↑ glecaprevir ↑ pibrentasvir	Coadministration is not recommended.
efavirenz	↓ glecaprevir ↓ pibrentasvir	Coadministration may lead to reduced antiviral efficacy and is not recommended.
HMG-CoA Reductase Inhibitors: atorvastatin, lovastatin simvastatin	↑ atorvastatin ↑ lovastatin ↑ simvastatin	Coadministration may increase the concentration of atorvastatin, lovastatin, and simvastatin, leading to an increased risk of myopathy, including rhabdomyolysis. Coadministration is not recommended.
pravastatin	↑ pravastatin	Coadministration may increase the concentration of pravastatin, leading to increased risk of myopathy, including rhabdomyolysis. Reduce pravastatin dose by 50%.
rosuvastatin	↑ rosuvastatin	Coadministration may significantly increase the concentration of rosuvastatin, leading to increased risk of

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
fluvastatin, pitavastatin	↑ fluvastatin ↑ pitavastatin	myopathy, including rhabdomyolysis. Rosuvastatin dose should not exceed 10 mg. Coadministration may increase the concentrations of fluvastatin and pitavastatin, leading to increased risk of myopathy, including rhabdomyolysis. Use the lowest necessary statin dose based on a risk/benefit assessment.
Immunosuppressants: cyclosporine	↑ glecaprevir ↑ pibrentasvir	Coadministration is not recommended in patients requiring stable cyclosporine doses >100 mg/day.

Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)
Please use the following table **AND** http://www.hep-druginteractions.org/checker to screen for drug interactions.

Vosevi® may be safely coadministered with any of the following drugs/combinations:

- Edurant® (rilpivirine)
- Epivir® (lamivudine)
- Ethinyl estradiol/norgestimate
- Emtriva® (emtricitabine)
- Descovy® (emtricitabine/tenofovir alafenamide)
- Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) – monitor for hepatic toxicity
- Isentress® (raltegravir)
- Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide)
- Prezista® (darunavir) with ritonavir (monitor for hepatic toxicity)
- Tivicay® (dolutegravir)

Drug Interactions (Not All Inclusive)

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
H_2-receptor antagonists (e.g., famotidine)	↓ velpatasvir	H_2-receptor antagonist doses greater than famotidine 40 mg twice daily (or equivalent H_2-receptor antagonist) may decrease ledipasvir concentration.

H_2 antagonist	Comparable dose
Tagamet® (cimetidine)	400 mg to 800 mg twice daily
Pepcid® (famotidine)	40 mg twice daily
Axid® (nizatidine)	300 mg twice daily
Zantac® (ranitidine)	150 mg four times daily

Proton-pump inhibitors (PPI): (e.g., omeprazole)	↓ velpatasvir	Omeprazole 20 mg can be administered with Vosevi® (sofosbuvir/velpatasvir/voxilaprevir). Although, use with other PPIs has not been studied, concomitant use with other PPI at a dose equivalent to omeprazole 20 mg is reasonable per European labeling.

Proton-pump inhibitor	Comparable dose
Aciphex® (rabeprazole)	20 mg

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
		Dexilant® (dexlansoprazole) 30 mg Nexium® (esomeprazole) 20 mg Prevacid® (lansoprazole) 30 mg Prilosec® (omeprazole) 20 mg Protonix® (pantoprazole) 40 mg
Antiarrhythmics: amiodarone	Unknown	Coadministration with of amiodarone may result in serious symptomatic bradycardia and is not recommended; if coadministration is required, cardiac monitoring is recommended.
Antiarrhythmics: digoxin	↑ digoxin	Coadministration with digoxin may increase the concentration of digoxin. Monitor therapeutic concentration of digoxin during coadministration.
Anticoagulants: dabigatran etexilate	↑ dabigatran	Coadministration necessitates clinical monitoring of dabigatran.
Anticonvulsants: carbamazepine, phenytoin, phenobarbital, oxcarbazepine	↓ sofosbuvir ↓ velpatasvir ↓ voxilaprevir	Coadministration is not recommended.
Antimycobacterial: rifampin	↓ sofosbuvir ↓ velpatasvir ↑ voxilaprevir (single dose) ↓ voxilaprevir (multiple dose)	Coadministration with rifampin is contraindicated.
rifabutin, rifapentine	↓ sofosbuvir ↓ velpatasvir ↓ voxilaprevir	Coadministration is not recommended.
Antiretrovirals: atazanavir lopinavir	↑ voxilaprevir	Coadministration with atazanavir- or lopinavir-containing regimens is not recommended.
tipranavir/ritonavir	↓ sofosbuvir ↓ velpatasvir	Coadministration with tipranavir/ritonavir is not recommended; the effect on voxilaprevir is unknown.
efavirenz, etravirine, nevirapine	↓ velpatasvir ↓ voxilaprevir	Coadministration with efavirenz, etravirine, and nevirapine-containing regimens is not recommended.
tenofovir disoproxil fumarate	↑ tenofovir	Avoid Vosevi® use if CrCl<60 mL/min. If coadministration is necessary, monitor for tenofovir-associated adverse reactions. **Drug interaction is avoided with these alternatives:** Descovy® (emtricitabine/tenofovir alafenamide)

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
		Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide)
St. John's wort	↓ sofosbuvir ↓ velpatasvir ↓ voxilaprevir	Coadministration is not recommended.
HMG-CoA Reductase Inhibitors: Pravastatin rosuvastatin pitavastatin atorvastatin fluvastatin lovastatin simvastatin	↑ pravastatin ↑ rosuvastatin ↑ pitavastatin ↑ atorvastatin ↑ fluvastatin ↑ lovastatin ↑ simvastatin	Coadministration increases the concentration of pravastatin, which is associated with increased risk of myopathy, including rhabdomyolysis. Pravastatin dose should not exceed 40 mg. Coadministration may significantly increase the concentration of rosuvastatin, which is associated with increased risk of myopathy, including rhabdomyolysis. Coadministration is not recommended. Coadministration may increase the concentration of pitavastatin and is not recommended, due to an increased risk of myopathy, including rhabdomyolysis. Coadministration may increase the concentrations of atorvastatin, fluvastatin, lovastatin, and simvastatin, which may increase the risk of myopathy, including rhabdomyolysis. It is recommended to use the lowest necessary statin dose based on a risk/benefit assessment.
Immunosuppressants: cyclosporine	↑ voxilaprevir	Coadministration increases the plasma concentration of voxilaprevir, the safety of which has not been established. Coadministration is not recommended.

Zepatier® (elbasvir/grazoprevir)

Zepatier® may be safely coadministered with any of the following drugs:

- Acid reducing agents (proton pump inhibitors, H_2 blockers, antacids)
- Edurant® (rilpivirine)
- Emtriva® (emtricitabine)
- Epivir® (lamivudine)
- Fuzeon® (enfuvirtide)
- Isentress® (raltegravir)
- Triumeq® (dolutegravir)
- Viread® (tenofovir disoproxil fumarate)
- Ziagen® (abacavir)

Drug Interactions (Not All Inclusive)

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
Antibiotics		

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
Nafcillin	↓ elbasvir ↓ grazoprevir	Reduced therapeutic activity of HCV regimen; co-administration is not recommended.
Anticonvulsants		
Phenytoin, carbamazepine	↓ elbasvir ↓ grazoprevir	Loss of therapeutic activity of HCV regimen; contraindicated.
Antifungals		
Ketoconazole	↑ elbasvir ↑ grazoprevir	Concomitant use with systemic ketoconazole increases grazoprevir exposure and may increase the overall risk of hepatotoxicity; coadministration is not recommended.
Antimycobacterials		
Rifampin	↓ elbasvir ↓ grazoprevir	Loss of therapeutic activity of HCV regimen; contraindicated.
Endothelin Antagonists		
Bosentan	↓ elbasvir ↓ grazoprevir	Reduced therapeutic activity of HCV regimen; co-administration is not recommended.
Herbal products		
St. John's Wort	↓ elbasvir ↓ grazoprevir	Loss of therapeutic activity of HCV regimen; contraindicated.
HIV Medications		
Atazanavir, darunavir, lopinavir, saquinavir, tipranavir	↑ grazoprevir	May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition. Contraindicated.
Efavirenz	↓ elbasvir ↓ grazoprevir	Loss of therapeutic activity of HCV regimen; contraindicated.
Elvitegravir/cobicistat/ emtricitabine/tenofovir (disoproxil fumarate or alafenamide)	↑ elbasvir ↑ grazoprevir	Increased concentrations of elbasvir and grazoprevir. Co-administration is not recommended.
Etravirine	↓ elbasvir ↓ grazoprevir	Reduced therapeutic activity of HCV regimen; co-administration is not recommended.
Nevirapine	Unknown	Coadministration is not recommended by AASLD/IDSA.
HMG-CoA Reductase Inhibitors		
Atorvastatin	↑ atorvastatin	Co-administration increases atorvastatin levels. Atorvastatin dose should not exceed 20 mg/day.
Fluvastatin, lovastatin, simvastatin	↑ fluvastatin, ↑ lovastatin, ↑ simvastatin	Co-administration has not been studied but may increase the concentrations of these statins. Closely monitor for statin-associated adverse events such as myopathy and use the lowest necessary dose.
Rosuvastatin	↑ rosuvastatin	Co-administration increases rosuvastatin levels. Rosuvastatin dose should not exceed 10 mg/day.
Immunosuppressants		
Cyclosporine	↑ grazoprevir	May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition. Contraindicated.

Concomitant Drug Class: Drug Name	Effect on Concentration	Recommendations
Tacrolimus	↑ tacrolimus	Frequent monitoring of tacrolimus whole blood concentrations, changes in renal function, and tacrolimus-associated adverse events upon the initiation of co-administration is recommended.
Wakefulness-Promoting Agents		
Modafinil	↓ elbasvir ↓ grazoprevir	Reduced therapeutic activity of HCV regimen; co-administration is not recommended.

Appendix B: Requests Noting Prior Failure with Mavyret® or Vosevi®
AASLD/IDSA Recommended Regimens in Patients with Prior Mavyret® or Vosevi® Failure

Genotype	Preferred Regimens
1, 2, 3, 4, 5, 6	Prior G/P failure G/P+SOF+RBV x 16 weeks (with or without CTP A cirrhosis) SOF/VEL/VOX x 12 weeks (no cirrhosis) or SOF/VEL/VOX+RBV x 12 weeks (CTP A cirrhosis) Prior SOF/VEL/VOX or G/P+SOF failure G/P+SOF+RBV x 16 weeks* (with or without CTP A cirrhosis) SOF/VEL/VOX+RBV x 24 weeks (with or without CTP A cirrhosis)

*Extension to 24 weeks should be considered in extremely difficult cases (e.g., genotype 3 with cirrhosis) or failure following G/P+SOF, but clinical data is not available to support this approach.
G/P=glecaprevir/pibrentasvir, RBV=ribavirin, SOF=sofosbuvir, VEL=velpatasvir, VOX=voxilaprevir

Requests documenting inability to differentiate prior treatment failure with DAA vs re-infection
If request documents that it is unclear whether the member failed prior treatment with DAA (e.g., treatment outcome is not available, viral load testing 12 weeks after treatment completion was not performed) or member achieved cure and was subsequently re-infected with HCV (e.g., via injection drug use), prescriber should repeat HCV genotype testing to guide HCV treatment selection:

- *If updated HCV genotype testing reveals the same genotype, this increases the likelihood of prior treatment failure with a DAA and member can be considered as having failed prior treatment for the purposes of PA review.*
- *If updated HCV genotype testing reveals a different genotype, it can be assumed that member's prior infection has been cured and member should be treated as if treatment-naïve (e.g., with sofosbuvir/velpatasvir, ledipasvir/sofosbuvir, or Mavyret®).*

Please use the following criteria to evaluate Mavyret® plus Sovaldi® plus ribavirin requests for members with prior Mavyret® or Vosevi® failure
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member ≥12 years of age (or <12 years of age and weight ≥45 kg)
4. Member has previously failed Mavyret® or Vosevi®
5. Requested regimen includes glecaprevir/pibrentasvir (three 100 mg/40 mg tablets once daily), sofosbuvir 400 mg once daily, and ribavirin

6. Requested duration is 16 weeks (24-week requests noting Vosevi® or (Mavyret® plus Sovaldi®) failure – Consult Clinical Reviewer)
7. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
8. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis) *Children <8 years old – See Appendix*
9. Member does not have decompensated cirrhosis (Child Pugh Class B or C)
10. Requested regimen does not have drug-drug interactions with member's concomitant medications

Please use the following criteria to evaluate Vosevi® requests for members with prior Mavyret® or Vosevi® failure
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member ≥18 years of age
4. **ONE** of the following
    a. **BOTH** of the following
        1. Member has previously failed Mavyret® and requested regimen is 400 mg/100 mg/100 mg once daily for 12 weeks
        2. For members with compensated cirrhosis, requested regimen includes ribavirin
    b. **ALL** of the following
        1. Member has previously failed Vosevi® or (Mavyret® plus Sovaldi®) and requested regimen is 400 mg/100 mg/100 mg once daily plus ribavirin for 24 weeks
        2. Clinical rationale for use instead of Mavyret® plus Sovaldi® plus ribavirin
5. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
6. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
7. Member does not have decompensated cirrhosis (Child Pugh Class B or C)
8. Requested regimen does not have drug-drug interactions with member's concomitant medications

Appendix C: Decompensated Cirrhosis (CTP Class B or C)

Decompensated cirrhosis includes any of the following complications: encephalopathy, variceal bleeding, ascites, jaundice, spontaneous bacterial peritonitis, HCC, hepatorenal syndrome, or hepatopulmonary syndrome (see table below). All requests for cirrhotic members should provide documentation of Child Pugh Class/score to distinguish compensated (Child Pugh Class A) vs decompensated cirrhosis (Child Pugh Class B or C).

Requests for members <18 years of age s/p liver transplant – ***Consult clinical reviewer.***

Metavir and Ishak Liver Fibrosis Staging Scales

METAVIR	ISHAK	Interpretation
Mild to moderate liver disease		
F0	**0**	No fibrosis
F1	**1,2**	Portal fibrosis without septa

F2	**3**	Few septa
Advanced liver disease		
F3	**4**	Numerous septa without cirrhosis
F4	**5,6**	Compensated cirrhosis (Child Pugh Class A)
F4 with complications	**5 or 6 with complications**	Decompensated cirrhosis (Child Pugh Class B or C) (suggested by the presence of encephalopathy, variceal hemorrhage, ascites, jaundice, spontaneous bacterial peritonitis, HCC, hepatorenal syndrome, or hepatopulmonary syndrome)

Child Turcotte Pugh (CTP) Classification of Cirrhosis Severity [click here for calculator]

	Class A	**Class B**	**Class C**
Total points	**5–6**	**7–9**	**10–15**
Factor	1 Point	2 points	3 points
Total bilirubin	<2 mg/dL	2-3 mg/dL (34-50 µmol/L)	>3 mg/dL (>50 µmol/L)
Serum albumin	>3.5 g/dL	2.8-3.5 g/dL (28-35 µmol/L)	<2.8 g/dL (<28 µmol/L)
INR	<1.7	1.7-2.3	>2.3
Ascites	None	Mild (or suppressed with medication)	Moderate to Severe
Hepatic encephalopathy	None	Grade I–II (or suppressed with medication)	Grade III–IV (or refractory)

AASLD/IDSA Recommended Regimens in Decompensated Cirrhosis (Child Pugh Class B or C)

Genotype	**Preferred Regimens**
1, 4, 5, or 6	LDV/SOF+RBV* x 12 weeks or LDV/SOF x 24 weeks (RBV ineligible) SOF/VEL+RBV* x 12 weeks or SOF/VEL x 24 weeks (RBV ineligible) Prior SOF or NS5A inhibitor failure LDV/SOF+RBV* x 24 weeks SOF/VEL+RBV* x 24 weeks
2 or 3	SOF/VEL+RBV* x 12 weeks or SOF/VEL x 24 weeks (RBV ineligible) Prior SOF or NS5A inhibitor failure SOF/VEL+RBV* x 24 weeks

LDV=ledipasvir, RBV=ribavirin, SOF=sofosbuvir, VEL=velpatasvir
*RBV starting dose is 600 mg and should be increased as tolerated.

Genotype 1, 2, 3, 4, 5, or 6
Please use the following criteria to evaluate sofosbuvir/velpatasvir requests:
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C
2. Genotype 1, 2, 3, 4, 5, or 6
3. Decompensated cirrhosis (Child Pugh Class B or C)
4. Member is not s/p liver or kidney transplant
5. Member is ≥3 years of age
6. Appropriate dosing
7. **ONE** of the following

a. Member is treatment-naïve or treatment-experienced (prior failure of peginterferon and ribavirin with or without an HCV protease inhibitor only) and **ONE** of the following:
    a. Requested regimen includes ribavirin and requested duration is 12 weeks
    b. Requested duration is 24 weeks and contraindication or prior intolerance to ribavirin
b. Member is treatment-experienced (prior failure of sofosbuvir- or NS5A inhibitor-containing regimen) and **BOTH** of the following:
    1. Requested regimen includes ribavirin
    2. Requested duration is 24 weeks

8. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
9. Requested regimen does not have drug-drug interactions with member's concomitant medications
10. If the request is for BRAND NAME Epclusa®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

Please use the following criteria to evaluate ledipasvir/sofosbuvir requests:
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C
2. Genotype 1, 4, 5 or 6
3. Member is ≥3 years of age
4. Appropriate dosing
5. Clinical rationale for use instead of sofosbuvir/velpatasvir
6. Decompensated cirrhosis (Child Pugh Class B or C)
7. Member is not s/p liver or kidney transplant
8. **ONE** of the following
    a. Member is treatment-naïve or treatment-experienced (prior failure of peginterferon and ribavirin with or without an HCV protease inhibitor only) and **ONE** of the following:
        a. Requested regimen includes ribavirin and requested duration is 12 weeks
        b. Requested duration is 24 weeks and contraindication or prior intolerance to ribavirin
    b. Member is treatment-experienced (prior failure of sofosbuvir- or NS5A inhibitor-containing regimen) and **BOTH** of the following:
        1. Requested regimen includes ribavirin
        2. Requested duration is 24 weeks
9. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
10. Requested regimen does not have drug-drug interactions with member's concomitant medications
11. If the request is for BRAND NAME Harvoni®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

Appendix D: Post-liver Transplant
Recurrence of HCV infection after liver transplantation is almost universal. For members with a recent liver transplant (e.g., within the last 1-2 years), fibrosis stage can generally be documented as early fibrosis, F0-F2 (fibrosis testing results are not required). However, if a specific fibrosis stage is documented in medical records or fibrosis testing results, document accordingly.

AASLD/IDSA Recommended Regimens in Liver Transplant Recipients

Genotype	Treatment Regimen
No prior DAA failure	
1, 4, 5, or 6	• G/P x 12 weeks (without cirrhosis) or G/P+RBV* x 12 weeks (CTP A cirrhosis plus other negative baseline factors) • LDV/SOF x 12 weeks (with or without CPT A cirrhosis) or LDV/SOF+RBV* x 12 weeks (treatment-naïve with CTP B or C cirrhosis) or LDV/SOF+RBV* x 24 weeks (treatment-experienced with CTP B or C cirrhosis) • SOF/VEL x 12 weeks (with or without CPT A cirrhosis) or SOF/VEL+RBV* x 12 weeks (treatment-naïve with CTP B or C cirrhosis) or SOF/VEL+RBV* x 24 weeks (treatment-experienced with CTP B or C cirrhosis)
2 or 3	• G/P x 12 weeks (without cirrhosis) or G/P+RBV* x 12 weeks (CTP A cirrhosis plus other negative baseline factors). FDA recommends 16 weeks in patients with genotype 3 who failed PEG/RBV ± SOF. • SOF/VEL x 12 weeks (with or without CPT A cirrhosis) or SOF/VEL+RBV* x 12 weeks (treatment-naïve with CTP B or C cirrhosis) or SOF/VEL+RBV* x 24 weeks (treatment-experienced with CTP B or C cirrhosis)
Prior DAA failure	
1, 2, 3, 4, 5, 6	• SOF/VEL/VOX x 12 weeks (DAA-experienced without CTP A cirrhosis) or SOF/VEL/VOX+RBV x 12 weeks (DAA-experienced with CTP A cirrhosis plus multiple negative baseline characteristics)

G/P=glecaprevir/pibrentasvir, DAA=direct-acting antiviral, LDV=ledipasvir, RBV=ribavirin, SOF=sofosbuvir, VEL=velpatasvir, VOX=voxilaprevir
*RBV starting dose is 600 mg (or lower if renal dysfunction) and should be increased as tolerated.

Genotype 1, 2, 3, 4, 5, 6
Please use the following criteria to evaluate Mavyret® requests:
Treatment-naïve members with or without compensated cirrhosis (CTP class A) - Use criteria in the procedure table to evaluate requests.

Treatment-experienced members (no prior NS5A failure) with or without compensated cirrhosis (CTP class A)

1. Diagnosis of hepatitis C and s/p liver transplant
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥3 years of age (or <12 years of age and weight ≥45 kg)
4. Appropriate dosing
5. For members with compensated cirrhosis (CTP A), requested regimen includes ribavirin *(Ribavirin may be bypassed on a case-by-case basis. If a clinical rationale is documented for not using ribavirin - Consult clinical reviewer)*
6. **ONE** of the following
    a. Genotype 1, 2, 4, 5, or 6 and requested duration is 12 weeks
    b. Genotype 3 (treatment-naïve only) and requested duration is 12 weeks
    c. Genotype 3 (prior failure of peginterferon/ribavirin with or without sofosbuvir) and requested duration is 16 weeks

7. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
8. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis) *Children <8 years old – See Appendix*
9. Requested regimen does not have drug-drug interactions with member's concomitant medications

Please use the following criteria to evaluate sofosbuvir/velpatasvir requests:
Treatment-naïve members with or without compensated cirrhosis (CTP class A) - Use procedure table criteria to evaluate requests

Treatment-experienced (failed peginterferon and ribavirin with or without an HCV protease inhibitor only) members with or without cirrhosis (CTP class A, B or C)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C and s/p liver transplant
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥3 years of age
4. Appropriate dosing
5. **ONE** of the following
    a. Absence of cirrhosis or compensated cirrhosis (CTP A) and requested duration is 12 weeks
    b. Decompensated cirrhosis (CTP B or C) and **BOTH** of the following:
        1. Requested regimen includes ribavirin
        2. Requested duration is 12 weeks (treatment-naïve) or 24 weeks (treatment-experienced)
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
7. If the request is for BRAND NAME Epclusa®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation
8. Requested regimen does not have drug-drug interactions with member's concomitant medications

Please use the following criteria to evaluate Vosevi® requests:
Treatment-experienced (failed treatment with sofosbuvir or an HCV NS5A inhibitor) members with or without compensated cirrhosis (CTP class A)
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatitis C and s/p liver transplant
2. **ONE** of the following
    a. Genotype 1, 2, 3, 4, 5, or 6 and prior treatment failure with an HCV NS5A inhibitor
    b. **ALL** of the following:
        1. Genotype 1 or 3 and prior treatment failure with sofosbuvir without an HCV NS5A inhibitor
        2. Clinical rationale for use instead of Mavyret®
    c. Genotype 4, 5, or 6 and prior treatment failure with sofosbuvir without an HCV NS5A inhibitor
3. Member ≥18 years of age
4. Requested dose is 400 mg/100 mg/100 mg once daily

5. For members with compensated cirrhosis (CTP A), requested regimen includes ribavirin
6. Requested duration is 12 weeks
7. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
8. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
9. Requested regimen does not have drug-drug interactions with member's concomitant medications

Requests for other regimens in members s/p liver transplant

- *Ledipasvir/sofosbuvir requests must provide clinical rationale for use instead of sofosbuvir/velpatasvir – Consult clinical reviewer if rationale is provided.*

Appendix E: Post-kidney Transplant[3]
AASLD/IDSA Preferred and Alternative Regimens in Kidney Transplant Recipients

Genotype	Treatment Regimen
No prior DAA	
Preferred Regimens	
1, 2, 3, 4, 5, 6	G/P x 12 weeks SOF/VEL x 12 weeks
1, 4, 5, 6	LDV/SOF x 12 weeks
Alternative Regimens	
1 or 4	EBR/GZR x 12 weeks (only for patients without baseline NS5A RASs)
Prior DAA	
1, 2, 3, 4, 5, 6	SOF/VEL/VOX x 12 weeks (no cirrhosis) or SOF/VEL/VOX+RBV x 12 weeks (CTP A cirrhosis plus other negative baseline factors)

EBR/GZR=elbasvir/grazoprevir, G/P=glecaprevir/pibrentasvir, LDV=ledipasvir, RAS=resistance-associated substitution, SOF=sofosbuvir, VEL=velpatasvir, VOX=voxilaprevir

Genotype 1, 2, 3, 4, 5, or 6:
Please use the following criteria to evaluate Mavyret® requests:
Treatment-naïve members with or without compensated cirrhosis (CTP class A) - Use procedure table criteria to evaluate requests

Treatment-experienced members (no prior NS5A failure) with or without compensated cirrhosis (CTP class A)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C and s/p kidney transplant
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥3 years of age
4. Appropriate dosing
5. Requested duration is 12 weeks*
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4) *Children <8 years old – See Appendix*
7. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis) *Children <8 years old – See Appendix*

8. Requested regimen does not have drug-drug interactions with member's concomitant medications

*Requests for 16-week treatment in genotype 3 patients who were treatment-experienced with peginterferon and/or ribavirin and/or sofosbuvir (without NS5A inhibitor) can be approved.

Please use the following criteria to evaluate sofosbuvir/velpatasvir requests:
Treatment-naïve members or treatment-experienced (failed peginterferon and ribavirin with or without an HCV protease inhibitor only) members with or without compensated cirrhosis (CTP class A)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C and s/p kidney transplant
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥3 years of age
4. Appropriate dosing
5. Requested duration is 12 weeks
6. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
7. Requested regimen does not have drug-drug interactions with member's concomitant medications
8. If the request is for BRAND NAME Epclusa®, member must meet the above criteria and the prescriber must provide medical records documenting an inadequate response or adverse reaction to the therapeutically equivalent generic formulation

Please use the following criteria to evaluate Vosevi® requests:
Treatment-experienced (failed treatment with sofosbuvir or an HCV NS5A inhibitor) members with or without compensated cirrhosis (CTP class A)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hepatitis C and s/p kidney transplant
2. Genotype 1, 2, 3, 4, 5, or 6
3. Member is ≥18 years of age
4. Requested dose is 400 mg/100 mg/100 mg once daily
5. For members with compensated cirrhosis (CTP A), requested regimen includes ribavirin *(Ribavirin may be bypassed on a case-by-case basis. If a clinical rationale is documented for not using ribavirin - Consult clinical reviewer)*
6. Requested duration is 12 weeks
7. Medical records and results of diagnostic tests assessing hepatic fibrosis including tests supporting liver disease staging (e.g., APRI, Fibroscan, Fibrosure, FIB-4)
8. Stage of liver disease is early stage (e.g., Metavir Score F0 to F2) or advanced stage (e.g., Metavir Score F3 to F4, documentation of cirrhosis)
9. Requested regimen does not have drug-drug interactions with member's concomitant medications

Requests for other regimens in members s/p kidney transplant

- *Ledipasvir/sofosbuvir requests must provide clinical rationale for use instead of sofosbuvir/velpatasvir – Consult clinical reviewer if rationale is provided.*
- *Zepatier® requests must provide clinical rationale for use instead of ledipasvir/sofosbuvir, sofosbuvir/velpatasvir, and Mavyret® – Consult clinical reviewer if considering an approval.*

Appendix F: HCV-Negative Organ Recipients from HCV-Positive Donors
With the limited availability of organ transplants, the use of HCV-positive donors has increased the donor pool and reduced waiting time. Treatment may be initiated immediately after transplantation without confirmation of viremia or obtaining recipient's genotype.

AASLD/IDSA Recommendations for HCV-Negative Organ Recipients from HCV-Positive Donors

Genotype	Treatment Regimen
Recommended Regimens	
1, 2, 3, 4, 5, 6	G/P x 12 weeks (liver transplant) or 8 weeks (non-liver solid organ transplant) SOF/VEL x 12 weeks
1, 4, 5, 6	LDV/SOF x 12 weeks
Alternative Regimen	
1, 4, 5, 6	LDV/SOF x 12 weeks
1 or 4	EBR/GZR x 12 weeks (only for patients without baseline NS5A RASs)

EBR/GZR=elbasvir/grazoprevir, G/P=glecaprevir/pibrentasvir, LDV=ledipasvir, RAS=resistance-associated substitution, SOF=sofosbuvir, VEL=velpatasvir

Genotype 1, 2, 3, 4, 5, or 6
Mavyret® or sofosbuvir/velpatasvir requests for treatment-naïve members with or without compensated cirrhosis (CTP class A) - *Use procedure table criteria to evaluate requests.*

- Mavyret® requests can be approved for 12 weeks (liver-transplant) or 8 weeks (non-liver solid organ transplant)
- Sofosbuvir/velpatasvir requests can be approved for 12 weeks

Requests for other regimens in HCV-positive donor recipients

- *Ledipasvir/sofosbuvir requests must provide clinical rationale for use instead of sofosbuvir/velpatasvir – Consult clinical reviewer if rationale is provided.*
- *Zepatier® requests must provide clinical rationale for use instead of ledipasvir/sofosbuvir, sofosbuvir/velpatasvir, and Mavyret® – Consult clinical reviewer if considering an approval.*

Appendix F: Laboratory Fibrosis Testing
Specific fibrosis stage (per lab report or clearly stated in medical records) may be required for all potential PA approvals for hepatitis C agents. MassHealth needs this information to better understand the population being treated. The goal is to differentiate early stage liver disease (F0-F2) from advanced (F3-F4). Thus, if the fibrosis stage falls solely into one group or the other, no additional testing is necessary for the purposes of documenting liver disease stage. However, additional testing to differentiate F3 from F4 may be required as part of the drug specific approval criteria.

Due to slow progression of liver disease in children, fibrosis testing is not required in young children (e.g., <8 years of age) unless there is evidence suggestive of decompensated cirrhosis.

According to the AASLD/IDSA guidelines, if any test below suggests cirrhosis, member should be treated as having cirrhosis.

Fibrosis Assessment	Cut Offs Suggesting Cirrhosis
APRI (AST to platelet ratio index)	>2.0
FIB-4	>3.25

Platelet count	<150,000/mm^3
FibroSure/FibroTest	F4
FibroScan stiffness	>12.5 kPa

Need for additional testing

1. *If specific fibrosis stage is not available or does not fall solely into F0-F2 or F3-F4 - additional testing is required. Serologic tests (e.g., Fibrosure) are readily available for this purpose.*
    a. *The following online calculators may be used in distinguishing F0-F2 from F3-F4*
        i. ***http://www.hepatitisc.uw.edu/page/clinical-calculators/apri***
            - *APRI >1.5 (=F3-F4)*
        ii. ***http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4***
            - *FIB-4<1.45 (=F0-F2) whereas FIB-4 >3.25 (=F4)*
    b. ***Additional testing to differentiate F3 from F4 may be required as part of the drug specific approval criteria***
2. *Radiologic testing documenting the presence of cirrhosis (e.g., FibroScan, ultrasound, MRI) is sufficient.*
3. *In general, if the fibrosis testing was performed >4-5 years ago documenting any stage between F0-F3, repeat testing is required as the member's liver disease may have progressed since then;* ***however, if prior testing confirmed cirrhosis (F4) – no additional more recent testing is required.*** *Documentation of Child Pugh Class is required for all members with cirrhosis.*

References

1. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.
2. Recommendations for testing, managing and treating Hepatitis C. (AASLD) (IDSA) Revised September 21, 2017. Guideline available at: http://www.hcvguidelines.org/.

Review History

11/20/2019 – Reviewed; updates to MH PD
11/18/2020 – Reviewed; separated out Comm/Exch vs. MH; no clinical changes
01/19/2022 – reviewed and Updated for Jan P&T; added Epclusa 150mg/37.5mg oral pellet to criteria and may be dispensed for age 3 to 5. Sofosbuvir/velpatasvir will continue to be preferred drug. New strength of Epclusa 150mg/37.5mg oral pellet is not available as generic at this time.
03/16/2022 – Reviewed and Updated for March P&T; Matched MH UPPL; Guideline updated to reflect new approval criteria for both Mavyret® (glecaprevir/pibrentasvir) and Epclusa® (sofosbuvir/velpatasvir) based on updated age indication. Multiple appendices updated to reflect changes. Effective 05/01/2022

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