Mass General Brigham
Health Plan

Hepatitis C Medications
Effective 04/01/2022

Plan	☐ MassHealth UPPL ☒Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit (NLX)		
Specialty Limitations	This medication has 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 Commercial and Exchange members:
Brand Name Harvoni™ (all dosage forms including pellets) **is the preferred combination agent HCV medication for Genotypes 1, 4, 5, and 6**
Brand Name Epclusa® (all dosage forms including oral pellets**) is the preferred combination agent HCV medication for Genotypes 2 and 3**
Vosevi™ is a non-preferred agent for Genotypes 1-6 previously treated with an NS5A inhibitor OR regimen of Sovaldi (sofosbuvir) without an NS5A inhibitor.
Current prior authorizations will be grandfathered for the life of the prior authorization
Sovaldi is a single agent formulary product for genotypes 1,4,5 & 6

NOTE: **Requests for Sovaldi (all dosage forms including pellets)** will be reviewed on a case-by-case basis taking into consideration medical necessity for use over a standard of care regimen. Sovaldi (sofosbuvir) plus peginterferon alfa and ribavirin and/or Sovaldi (sofosbuvir) plus ribavirin are not currently recommended by AASLD-IDSA treatment guidelines for routine use in the treatment of hepatitis C.

Mass General Brigham Health Plan will continue to review non-preferred products on a case by case basis and cover when medically necessary.

All Hepatitis C medications are specialty products; dispensing is available only when obtained from any contracted specialty pharmacy including CVS Caremark Specialty Pharmacy.

NOTE: FDA has received reports that the use of Mavyret, Zepatier, or Vosevi to treat chronic Hepatitis C in patients with moderate to severe liver impairment has resulted in rare cases of worsening liver function or liver failure. Mavyret and Zepatier should not be prescribed in patients with any history of prior hepatic decompensation. Vosevi is indicated for patients who have previously failed certain other Hepatitis C Virus treatments and is not recommended in patients with any history of hepatic decompensation unless the benefits outweigh the risk of liver injury, liver failure or death.

Mass General Brigham Health Plan will continue to review non-preferred products on a case by case basis and cover when medically necessary.

Coverage Guidelines
Approval will be granted if the member meets all following criteria and documentation has been submitted:

Approvable Diagnosis

- Chronic hepatitis C (CHC) infection
- Member is new to the plan and has already been started and stabilized on a regimen of hepatitis C medication(s) as part of an appropriate treatment regimen (e.g. genotype, combination therapy, dose, treatment duration, etc.) for chronic hepatitis C infection

OR

- Member has a diagnosis of chronic hepatitis C (CHC) infection **AND**
- Member has a detectable HCV RNA viral load drawn from within the last 6 months **AND**
- Member has documented liver disease **AND**
- Member has documentation of stage of hepatic fibrosis through one of the following:
    - Liver biopsy confirming a Metavir stage
    - Transient elastography (FibroScan®) score
    - Fibrotest (such as FibroSureTM) score
    - AST to Platelet Ratio Index (APRI) score
    - Severe extra hepatic manifestations/symptoms

OR

- Member has failed previous treatment with an NS5A inhibitor OR regimen of sofosbuvir without an NS5A inhibitor **AND**
- Member has a diagnosis of chronic hepatitis C (CHC) infection **AND**
- Member has a detectable HCV RNA viral load drawn from within the last 6 months **AND**
- Member has documented liver disease **AND**
- Member has documentation of stage of hepatic fibrosis through one of the following:
    - Liver biopsy confirming a Metavir stage
    - Transient elastography (FibroScan®) score
    - Fibrotest (such as FibroSureTM) score
    - AST to Platelet Ratio Index (APRI) score
    - Severe extra hepatic manifestations/symptoms

AND all of the following:

- Member has demonstrated understanding of the proposed treatment plan and has displayed the ability to adhere to medications and clinical appointments **AND**
- The requested dose and duration of therapy are consistent with published label indications for each medication and the AASLD published treatment guidelines, management in Tables 1 through 3.
- Provider will submit HCV RNA viral load 12 weeks (SVR12) after completion of therapy to assess virologic cure.

- For therapies exceeding 12 weeks, provider will submit HCV RNA viral load at week 4 of treatment. Repeat HCV RNA should be drawn at 6 week if viral load is detectable at week 4.
- All other requests will be reviewed on a case-by-case basis consistent with approved FDA labeling and/or recognized treatment guidelines.

Limitations:

Table 1: Hepatitis C Regimens for Treatment-Naïve Patients and Treatment Experienced Patients by Genotype

Genotype	Treatment History			Regimen	Duration
Genotype 1A With compensated cirrhosis	Treatment Naïve		Without cirrhosis	Daily Zepatier (without baseline NS5A polymorphisms) **Class I, Level A**	12 weeks
				Daily Harvoni **Class I, Level A** *HCV RNA <6,000,000 IU/mL (8 weeks) *HCV RNA >6,000,000 IU/mL (12 weeks)	8-12 weeks*
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	8 weeks
			With compensated cirrhosis	Daily Zepatier (without baseline NS5A polymorphisms) **Class I, Level A**	12 weeks
				Daily Harvoni **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	12 weeks
	Treatment Experienced	Prior PEG-IFN + RBV failed	Without cirrhosis	Daily Zepatier (without baseline NS5A polymorphisms) **Class I, Level A**	12 weeks
				Daily Harvoni **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	8 weeks
			With compensated cirrhosis	Daily Zepatier (without baseline NS5A polymorphisms) **Class I, Level A**	12 weeks
				Daily Harvoni + weight-based ribavirin **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level B**	12 weeks
		Prior sofosbuvir plus RBV +/- PEG-INF regimen failed	Without cirrhosis	Daily Vosevi **Class I, Level A**	12 weeks
				Daily Harvoni + weight-based ribavirin **Class IIa, Level B**	12 weeks
				Daily Mavyret **Class IIa, Level B**	12 weeks
			With compensated cirrhosis	Daily Vosevi **Class I, Level A**	12 weeks
				Daily Harvoni + weight-based ribavirin **Class IIa, Level B**	24 weeks
				Daily Mavyret **Class IIa, Level B**	12 weeks
		Prior NS3 PI (telaprevir, boceprevir, or simeprevir) + PEG-INF/RBV regimen failed	Without cirrhosis	Daily Harvoni **Class I, Level A**	12 weeks
				DailyEpclusa **Class1 Level B**	12 weeks
				Daily Mavyret **Class IIa, Level B**	12 weeks
			With compens	Daily Harvoni + weight-based ribavirin **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks

			ated cirrhosis	Daily Mavyret **Class IIa, Level B**	12 weeks
		Prior NS5A inhibitor regimen failed≠	**+/- cirrhosis**	Daily Vosevi **Class I, Level A**	12 weeks
				Daily Vosevi **Class I, Level A**	12 weeks
Genotype 1b	**Treatment Naïve**		**Without cirrhosis**	Daily Zepatier **Class I, Level A**	12 weeks
				Daily Harvoni **Class I, Level A** *HCV RNA <6,000,000 IU/mL (8 weeks) *HCV RNA >6,000,000 IU/mL (12 weeks)	8-12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	8 weeks
			With compensated cirrhosis	Daily Zepatier **Class I, Level A**	12 weeks
				Daily Harvoni **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	12 weeks
	Treatment Experienced	**Prior PEG-IFN + RBV failed**	**Without cirrhosis**	Daily Zepatier **Class I, Level A**	12 weeks
				Daily Harvoni **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	8 weeks
			With compensated cirrhosis	Daily Zepatier **Class I, Level A**	12 weeks
				Daily Harvoni + weight based ribavirin **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level B**	12 weeks
		Prior sofosbuvir plus RBV +/- PEG-INF regimen failed	**Without cirrhosis**	Daily Harvoni + weight-based ribavirin **Class IIa, Level B** Daily Mavyret **Class IIa, Level B**	12 weeks 12 weeks
			With compensated cirrhosis	Daily Harvoni + weight-based ribavirin **Class IIa, Level B** Daily Mavyret **Class IIa, Level B**	24 weeks 12 weeks
		Prior NS3 PI (telaprevir, boceprevir, or simeprevir) + PEG-INF/RBV regimen failed	**Without cirrhosis**	Daily Harvoni **Class I, Level A**	12 weeks
				Daily **Class I, Level A**	12 weeks
				Daily Mavyret **Class IIa, Level B**	12 weeks
			With compensated cirrhosis	Daily Harvoni + weight-based ribavirin **Class I, Level A**	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class IIa, Level B**	12 weeks
		Prior NS5A inhibitor	**Without cirrhosis**	Daily Vosevi **Class I, Level A**	12 weeks

		regimen failed≠	**With compensated cirrhosis**	Daily Vosevi **Class I, Level A**	12 weeks

*Shortening treatment of Harvoni to 8 weeks is not recommended for HIV co-infected patients, African-American patients, or those with known IL28B polymorphism CT or TT.

≠ NS5A inhibitors single agents: 1) Daklinza, 2) ombitasvir in Viekira-Pak, 3) ledipasvir in Harvoni, and 4) elbasvir in Zepatier.
ΔThe concomitant use of Daklinza (daclatasvir) with cytochrome P450 3A/4 inducers and inhibitors may require a dose adjustment.

Genotype 2	**Treatment naïve**		**Without cirrhosis**	Daily Epclusa **Class I, Level A** Daily Mavyret **Class I, Level A**	12 weeks 8 weeks
			With compensated cirrhosis	Daily Epclusa **Class I, Level A** Daily Mavyret **Class I, Level A**	12 weeks 12 weeks
	Treatment Experienced	**Prior PEG-IFN + RBV failed**	**Without cirrhosis**	Daily Epclusa **Class I, Level A** Daily Mavyret **Class I, Level A**	12 weeks 8 weeks
			With compensated cirrhosis	Daily Epclusa **Class I, Level A** Daily Mavyret **Class I, Level B**	12 weeks 12 weeks
		Prior sofosbuvir + RBV failed	**+/- compensated cirrhosis**	Daily Epclusa + weight based ribavirin **Class IIa, Level C** Daily Mavyret **Class IIb, Level B**	12 weeks 12 weeks
Genotype 3	**Treatment naïve**		**Without cirrhosis**	Daily Sovaldi + Daklinza **Class I, Level A**Δ	12 weeks
				Daily Epclusa **Class I, Level A**	12 weeks
				Daily Mavyret **Class I, Level A**	8 weeks
			With compensated cirrhosis	Daily Epclusa **Class I, Level A**¶ Daily Mavyret **Class I, Level A**	12 weeks 12 weeks
	Treatment Experienced	**Prior PEG-IFN + RBV failed**	**Without cirrhosis**¶	Daily Sovaldi + Daklinza **Class I, Level A**Δ¶	12 weeks
				Daily Epclusa **Class I, Level A**¶	12 weeks
				Daily Vosevi **Class IIa, Level B** if Y93M mutation is present	12 weeks
				Daily Mavyret **Class IIa, Level B**	16 weeks
			With compensated cirrhosis	Daily Epclusa + weight based ribavirin **Class I, Level B** Daily Mavyret **Class IIa, Level B**	12 weeks 16 weeks
		Prior sofosbuvir + RBV failed	**+/- compensated cirrhosis**	Daily Epclusa + weight based ribavirin **Class IIa, Level C**	12 weeks
		Prior NS5A inhibitor Regimen failed	**+/- compensated cirrhosis**	Daily Vosevi **Class I, Level A**	12 weeks
				Daily Vosevi +RBV **Class IIa, Level C**	12 weeks

ΔThe concomitant use of Daklinza (daclatasvir) with cytochrome P450 3A/4 inducers and inhibitors may require a dose adjustment.
¶RAV testing for Y93H is recommended and ribavirin should be included if present.

Genotype 4	**Treatment naïve**	**+/- compensated cirrhosis**	Daily Epclusa **Class I, Level A**	12 weeks
			Daily Zepatier **Class IIa, Level B**	12 weeks
			Daily Harvoni **Class IIa, Level B**	12 weeks

				Daily Mavyret **Class I, Level A** Without Cirrhosis*	8 weeks*
				Daily Mavyret **Class I, Level B** With Cirrhosis*	12 weeks*
	Treatment Experienced	**Prior PEG-IFN + RBV failed**	**Without cirrhosis**	Daily Epclusa **Class I, Level A**	12 weeks
				Daily Harvoni **Class IIa, Level B**	8 weeks
				Daily Mavyret **Class I, Level B**	8 weeks
			With compensated cirrhosis	Daily Epclusa **Class I, Level A**	12 weeks
				Daily Harvoni + weight based ribavirin (if ribavirin eligible) **Class IIa, Level B**	12 weeks
				Daily Mavyret **Class IIa, Level B**	12 weeks
		Prior NS5A inhibitor regimen failed	**+/- compensated cirrhosis**	Daily Vosevi **Class I, Level A**	12 weeks
Genotype 5	**Treatment Naïve**		**+/- compensated cirrhosis**	Daily Epclusa **Class I, Level A**	12 weeks
				Daily Harvoni **Class IIa, Level B**	12 weeks
				Daily Mavyret **Class I, Level A** * Without Cirrhosis (8 weeks) * With Compensated Cirrhosis (12 weeks)	8 - 12 weeks*
	Treatment Experienced		**Prior PEG-IFN + RBV failed**	Daily Epclusa **Class IIa, Level B**	12 weeks
				Daily Harvoni **Class IIa, Level C**	12 weeks
				Daily Mavyret **Class IIa, Level B*** *Without Cirrhosis	8 weeks
				Daily Mavyret **Class IIa, Level B*** *With Compensated Cirrhosis	12 weeks
			Prior NS5A inhibitor regimen failed	Daily Vosevi **Class IIa, Level B**	12 weeks
Genotype 6	**Treatment naïve**		**+/- compensated cirrhosis**	Daily Epclusa **Class I, Level A**	12 weeks
				Daily Harvoni **Class IIa, Level B**	12 weeks
				Daily Mavyret **Class I, Level A*** *Without Cirrhosis (8 weeks) *With Compensated Cirrhosis (12 weeks)	8 - 12 weeks*
	Treatment Experienced		**Prior PEG-IFN + RBV failed**	Daily Epclusa **Class IIa, Level B**	12 weeks
				Daily Harvoni **Class IIa, Level C**	12 weeks
				Daily Mavyret **Class IIa, Level B*** *Without Cirrhosis	8 weeks
				Daily Mavyret **Class IIa, Level B** *With Compensated Cirrhosis	12 weeks
			Prior NS5A inhibitor regimen failed	Daily Vosevi **Class IIa, Level B**	12 weeks

Table 2: Hepatitis C Regimens for HIV/HCV Co-Infected Patients

Antiretroviral drug switches, when needed, should be done in collaboration with the HIV practitioner. For HIV antiretroviral and HCV direct-acting antiviral combinations not addressed below, expert consultation is recommended. **Class I, Level A**

Daklinza requires dose adjustment with ritonavir-boosted atazanavir (a decrease to 30mg daily) and efavirenz or etravirine (an increase to 90mg daily). Class **IIa, Level B**
Zepatier should be used with antiretroviral drugs which it does not have clinically significant interactions: abacavir, emtricitabine, enfuvirtide, lamivudine, raltegravir, dolutegravir, rilpivirine, and tenofovir. **Class IIa, Level B**
Olysio should be used with antiretroviral drugs with which it does not have clinically significant interactions: abacavir, emtricitabine, enfuvirtide, lamivudine, maraviroc, raltegravir, (and probably dolutegravir), rilpivirine, and tenofovir. **Class IIa, Level B**
Velpatasvir increases tenofovir levels; therefore, concomitant use with sofosbuvir/velpatasvir (Epclusa) mandates consideration of renal function and should be avoided in those with CrCl below 60 mL/min. In patients with CrCl > 60 mL/min concomitant dosing of velpatasvir and TDF with ritonavir-boosted or cobicistat-boosted regimens did not result in renal toxicity in 56 subjects. Renal monitoring is recommended during the dosing period. Tenofovir alafenamide (TAF) may be an alternative to TDF during sofosbuvir/velpatasvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy. **Class IIa, Level B**
Fixed-dose combination of Harvoni (ledipasvir/sofosbuvir) increases tenofovir levels; therefore, concomitant use mandates consideration of creatinine clearance (CrCl) rate and should be avoided in those with CrCl <60 mL/min. Because potentiation of this effect is expected when tenofovir is used with ritonavir-boosted or cobicistat-boosted regimens, ledipasvir should be avoided with this combination (pending further data) unless antiretroviral regimen cannot be changed and the urgency of treatment is high. For combinations expected to increase tenofovir levels, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended. Tenofovir alafenamide (TAF) may be an alternative to TDF during ledipasvir/sofosbuvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy. **Class IIa, Level C**
For combinations expected to increase tenofovir levels, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended. **Class Iia, Level C**
Viekira Pak should be used with antiretroviral drugs with which they do not have substantial interactions: atazanavir, dolutegravir, emtricitabine, enfuvirtide, lamivudine, raltegravir, and tenofovir. The dose of ritonavir used for boosting of HIV protease inhibitors may need to be adjusted (or held) when administered with Viekira Pak and then restored when HCV treatment is completed. The HIV protease inhibitor should be administered at the same time as the fixed-dose HCV combination. **Class IIa, Level C**

Notes

- Non-responders (or null responders) are defined as those who experienced less than a 2 log decline in viral load during a previous 12 week treatment course (viral load was never undetectable). Partial responders experienced greater viral load suppression than non- responders, but viral load was never undetectable during treatment. These individuals have lower re-treatment success.
- Relapsers are defined as those who achieved undetectable HCV RNA blood levels during previous treatment who relapsed after treatment cessation. Relapsers should be treated as if they are naïve to therapy. These individuals tend to do well with re-treatment.
- For patients who are currently taking an antacid, H2 antagonist, or proton pump inhibitor and require a sofosbuvir/velpatasvir - or ledipasvir/sofosbuvir -containing regimen, Mass General Brigham Health Plan requires documentation of how this drug interaction will be managed.

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
Reviewed 11/20/19 (updates to MH PD)
11/18/2020 – Reviewed and Updated; separated out MH vs. Comm/Exch
01/19/2022 – Reviewed and Updated; added Epclusa oral pellet to criteria as preferred for Genotype 2 and 3. Effective 04/01/2022.