Treatment Guidelines

HEPATITIS C

PANGENOTYPIC

EPCLUSA		
Patient population	**Treatment**	**Duration**
Without cirrhosis and with compensated (child-Pugh A) cirrhosis	Epclusa	12 weeks
With decompensated (child-Pugh B or C) cirrhosis	Epclusa + ribavirin*	12 weeks

* When administered with EPCLUSA, the recommended dosage of ribavirin is based on weight (administered with food): 1000 mg per day for patients less than 75 kg and 1200 mg for those weighing at least 75 kg, divided and administered twice daily. The starting dosage and on-treatment dosage of ribavirin can be decreased based on hemoglobin and creatinine clearance. For ribavirin dosage modifications, refer to the ribavirin prescribing information.

- No dosage recommendation can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate [eGFR] less than 30 mL/min/1.73m2) or with end stage renal disease (ESRD), due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite [see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]
- Serious Symptomatic Bradycardia When Sofosbuvir Is Coadministered with Amiodarone and Another HCV Direct-Acting Antiviral
- that are inducers of P-gp and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4 (e.g., rifampin, St. John's wort, carbamazepine) may significantly decrease plasma concentrations of sofosbuvir and/or velpatasvir, leading to potentially reduced therapeutic effect of EPCLUSA. The use of these agents with the EPCLUSA is not recommended [see Drug Interactions (7.3)]
- If administered with ribavirin the warnings and precautions for ribavirin will apply to the combination.
- HCV/HIV-1 coinfection: For patients with HCV/HIV-1 coinfection, follow the dosage recommendations in the table above.

MAVYRET		
Patient population	**Treatment**	**Duration**
All Genotypes		
Treatment-naïve with or without compensated cirrhosis (child-pugh A)	Mavyret	8 weeks
Genotype 1		
Previously treated with a regimen containing an NS5A inhibitor* without prior treatment with an NS3/4A protease inhibitor	Mavyret	without cirrhosis: 16 weeks compensated cirrhosis (child-Pugh A): 16 weeks
Previously treated with a regimen containing an NS3/4A PI** without prior treatment with an NS5A inhibitor	Mavyret	without cirrhosis: 12 weeks compensated cirrhosis (child-Pugh A): 12 weeks
Genotype 1, 2, 4, 5, 6		
PRS	Mavyret	without cirrhosis: 8 weeks compensated cirrhosis (child-Pugh A): 12 weeks
Genotype 3		
PRS†	Mavyret	without cirrhosis: 16 weeks compensated cirrhosis (child-Pugh A): 16 weeks

* In clinical trials, subjects were treated with prior regimens containing ledipasvir and sofosbuvir or daclatasvir with pegylated interferon and ribavirin.
** In clinical trials, subjects were treated with prior regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with pegylated interferon and ribavirin.
† PRS=Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor.

PANGENOTYPIC

VOSEVI		
Patient population	**Treatment**	**Duration**
All Genotypes		
Adults with chronic hepatitis C virus infection without cirrhosis or with compensated cirrhosis who were previously treated with an NS5A inhibitor	Vosevi*	12 weeks
Genotype 1a, 3		
Adults with chronic hepatitis C virus infection without cirrhosis or with compensated cirrhosis who were previously treated with sofosbuvir without an NS5A inhibitor	Vosevi**	12 weeks

* In clinical trials, prior NS5A inhibitor experience included daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir.
** In clinical trials, prior treatment experience included sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir).

Used for both NSFA inhibitors and Sofosbuvir with no NS5A. Use only for treatment experienced.

GENOTYPE 1

EPCLUSA
For Epclusa treatment information please refer to Eplusa in the Pangenotypic heading.

HARVONI		
Patient population	**Treatment**	**Duration**
Treatment-naive and experienced with decompensated cirrhosis	Harvoni + ribavirin	12 weeks
Transplant with or without cirrhosis	Harvoni + ribavirin	12 weeks
Treatment-naive with or without cirrhosis	Harvoni	12 weeks*
Treatment-experienced** without cirrhosis	Harvoni	12 weeks
Treatment-experienced** with cirrhosis	Harvoni	24 weeks

* HARVONI for 8 weeks can be considered in treatment-naive patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL [see Clinical Studies (14)].
** Treatment-experienced patients who have failed a peginterferon alfa + ribavirin based regimen with or without an HCV protease inhibitor.

MAVYRET
For Mavyret treatment information please refer to Mavyret in the Pangenotypic heading.

VOSEVI
For Vosevi treatment information please refer to Vosevi in the Pangenotypic heading.

GENOTYPE 1

ZEPATIER		
Patient population	**Treatment***	**Duration**
Genotype 1a: Treatment-naive or PegIFN/RBV-experienced* without baseline NS5A polymorphisms†	ZEPATIER	12 weeks
Genotype 1a: Treatment-naive or PegIFN/RBV-experienced* with baseline NS5A polymorphisms†	ZEPATIER + RBV‡	16 weeks
Genotype 1b: Treatment-naive or PegIFN/RBV-experienced*	ZEPATIER	12 weeks
Genotype 1a§ or 1b: PegIFN/RBV/PI-experienced¶	ZEPATIER + RBV‡	12 weeks
Genotype 4: Treatment-naive	ZEPATIER	12 weeks
Genotype 4: PegIFN/RBV-experienced*	ZEPATIER + RBV‡	16 weeks

* Patients who have failed treatment with peginterferon alfa (PegIFN) + ribavirin (RBV).
† NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93. See section 2.1 Testing prior to the initation of therapy, subsection NS5A resistance testing in HCV genotype 1a-infected patients.
‡ For patients with CrCl greater than 50 mL per minute, the recommended dosage of ribavirin is weight-based (less than 66 kg = 800 mg per day, 66 to 80 kg = 1000 mg per day, 81 to 105 kg = 1200 mg per day, greater than 105 kg = 1400 mg per day) administered in two divided doses with food. For patients with CrCl less than or equal to 50 mL per minute, including patients receiving hemodialysis, refer to the ribavirin tablet prescribing information for the correct ribavirin dosage.
§ The optimal ZEPATIER-based treatment regimen and duration of therapy for PegIFN/RBV/PI-experienced genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31, and 93 has not been established.
¶ Patients who have failed treatment with PegIFN + RBV + HCV NS3/4A protease inhibitor (PI): boceprevir, simeprevir, or telaprevir.

- For Genotype 1a patient needs NS5A testing
- HIV Co-Infected follow standard dosing according to above chart
- Renal Impairment DOES NOT require ZEPATIER dose adjustment – Ribavirin may still require dose adjustment
- Co-administration with CYP3A inducers OR inhibitors is not recommended

GENOTYPE 2 OR 3

EPCLUSA
For Epclusa treatment information please refer to Eplusa in the Pangenotypic heading.

MAVYRET
For Mavyret treatment information please refer to Mavyret in the Pangenotypic heading.

VOSEVI
For Vosevi treatment information please refer to Vosevi in the Pangenotypic heading.

GENOTYPE 4

EPCLUSA
For Epclusa treatment information please refer to Eplusa in the Pangenotypic heading.

HARVONI		
Patient population	**Treatment**	**Duration**
Treatment-naive and treatment-experienced*, with or without cirrhosis	Harvoni	12 weeks
Liver transplant with or without cirrhosis	Harvoni + ribavirin	12 weeks

* Treatment-experienced patients who have failed a peginterferon alfa + ribavirin based regimen with or without an HCV protease inhibitor.

- HCV/HIV-1 co-infection: For patients with HCV/HIV-1 co-infection, follow the dosage recommendations in the table above.

GENOTYPE 4

MAVYRET

For Mavyret treatment information please refer to Mavyret in the Pangenotypic heading.

VOSEVI

For Vosevi treatment information please refer to Vosevi in the Pangenotypic heading.

ZEPATIER

Patient population	Treatment*	Duration
Genotype 1a: Treatment-naive or PegIFN/RBV-experienced* without baseline NS5A polymorphisms†	ZEPATIER	12 weeks
Genotype 1a: Treatment-naive or PegIFN/RBV-experienced* with baseline NS5A polymorphisms†	ZEPATIER + RBV‡	16 weeks
Genotype 1b: Treatment-naive or PegIFN/RBV-experienced*	ZEPATIER	12 weeks
Genotype 1a§ or 1b: PegIFN/RBV/PI-experienced¶	ZEPATIER + RBV‡	12 weeks
Genotype 4: Treatment-naive	ZEPATIER	12 weeks
Genotype 4: PegIFN/RBV-experienced*	ZEPATIER + RBV‡	16 weeks

* Patients who have failed treatment with peginterferon alfa (PegIFN) + ribavirin (RBV).
† NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93. See section 2.1 Testing prior to the initation of therapy, subsection NS5A resistance testing in HCV genotype 1a-infected patients.
‡ For patients with CrCl greater than 50 mL per minute, the recommended dosage of ribavirin is weight-based (less than 66 kg = 800 mg per day, 66 to 80 kg = 1000 mg per day, 81 to 105 kg = 1200 mg per day, greater than 105 kg = 1400 mg per day) administered in two divided doses with food. For patients with CrCl less than or equal to 50 mL per minute, including patients receiving hemodialysis, refer to the ribavirin tablet prescribing information for the correct ribavirin dosage.
§ The optimal ZEPATIER-based treatment regimen and duration of therapy for PegIFN/RBV/PI-experienced genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31, and 93 has not been established.
¶ Patients who have failed treatment with PegIFN + RBV + HCV NS3/4A protease inhibitor (PI): boceprevir, simeprevir, or telaprevir.

- For Genotype 1a patient needs NS5A testing
- HIV Co-Infected follow standard dosing according to above chart
- Renal Impairment DOES NOT require ZEPATIER dose adjustment – Ribavirin may still require dose adjustment
- Co-administration with CYP3A inducers OR inhibitors is not recommended

GENOTYPE 5 OR 6

EPCLUSA

For Epclusa treatment information please refer to Eplusa in the Pangenotypic heading.

HARVONI

Patient population	Duration
Treatment-naive and treatment-experienced*, with or without cirrhosis	12 weeks

* Treatment-experienced patients who have failed a peginterferon alfa + ribavirin based regimen with or without an HCV protease inhibitor.

- HCV/HIV-1 co-infection: For patients with HCV/HIV-1 co-infection, follow the dosage recommendations in the table above.

MAVYRET

For Mavyret treatment information please refer to Mavyret in the Pangenotypic heading.

VOSEVI

For Vosevi treatment information please refer to Vosevi in the Pangenotypic heading.