Texas Vendor Drug Program

Drug Use Criteria: Hepatitis C Direct-Acting Antivirals

Publication History

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Notes: All criteria may be applied retrospectively. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.

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1 Dosage[1-14]

1.1 Adults

Direct acting antivirals (DAA) for hepatitis are FDA-indicated for treatment of chronic infections caused by hepatitis C virus (HCV). Individual agents have varying FDA indications and treatment durations based on genotype (1-6), subtype (1a vs. 1b), liver function, HIV co-infection and/or previous treatment history. While there are no FDA recommendations for renal adjustment with these agents, sofosbuvir metabolites do accumulate with impaired renal function. **DAAs used for chronic HCV infection are summarized in Tables 1-4. Dosages exceeding these recommendations will be reviewed.**

Table 1. DAAs for Treatment of Adult Chronic HCV Infection - Monotherapy

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1 or 3 without cirrhosis	daclatasvir (Daklinza®)	30 mg, 60 mg tablets	60 mg once daily	**sofosbuvir***
Chronic HCV infection genotype 1 or 3 with compensated cirrhosis (Child-Pugh A)			60 mg once daily	**sofosbuvir***
Chronic HCV infection genotype 1 or 3 with decompensated cirrhosis (Child-Pugh B or C)			60 mg once daily	**sofosbuvir + ribavirin***
Chronic HCV infection genotype 1 or 3 post-liver transplant			60 mg once daily	**sofosbuvir + ribavirin***
Chronic HCV infection genotype 1 and 4 treatment-naïve without cirrhosis	sofosbuvir (Sovaldi®)	400 mg tablets	One tablet once daily	**peginterferon alfa + ribavirin***

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1 treatment-naïve without cirrhosis unable to receive interferon products	sofosbuvir (Sovaldi®)	400 mg tablets	One tablet once daily	**daclatasvir or ribavirin***
Chronic HCV infection genotype 2 or 3 treatment-naïve without cirrhosis or those who have failed interferon + ribavirin			One tablet once daily	**ribavirin***
Chronic HCV infection genotype 1 and 4 with compensated cirrhosis (Child-Pugh A)			One tablet once daily	**peginterferon alfa + ribavirin***
Chronic HCV infection genotype 2 or 3 with compensated cirrhosis (Child-Pugh A)			One tablet once daily	**ribavirin***
Chronic HCV infection genotypes 1-4 with hepatocellular carcinoma awaiting liver transplantation			One tablet once daily	**ribavirin^**

HCV = hepatitis C virus

monotherapy agent that must be given in conjunction with other select antiviral(s) for optimal efficacy

^***patients unable to take ribavirin may receive daclatasvir as an alternative***

Table 2. DAAs for Treatment of Adult Chronic HCV Infection – Combination Therapy

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1a (**no baseline NS5A polymorphisms**), 1b, or 4 **treatment-naïve with or without cirrhosis**	elbasvir/ grazoprevir (Zepatier®)	50 mg/ 100 mg tablets	One tablet once daily	**---**
Chronic HCV infection genotype 1a (with baseline NS5A polymorphisms) treatment-naïve with or without cirrhosis			One tablet once daily	**ribavirin**
Chronic HCV infection genotype 1-6 without cirrhosis	glecaprevir/ pibrentasvir (Mavyret™)	100 mg/ 40 mg tablets	3 tablets with food once daily	**---**
Chronic HCV infection genotype 1-6 with compensated cirrhosis (Child-Pugh A)			3 tablets with food once daily	**---**
Chronic HCV infection genotype 1, 4, 5, or 6 **treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)**	ledipasvir/ sofosbuvir (Harvoni®, **generics**)	90 mg/ 400 mg tablets	One tablet once daily	
Chronic HCV infection genotype 1 **treatment-naïve** with decompensated cirrhosis (Child-Pugh B or C)			One tablet once daily	**ribavirin**

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1 or 4 post-transplant **with or without compensated cirrhosis (Child-Pugh A)**			One tablet once daily	**ribavirin**
Chronic HCV infection **genotype 1a with or without cirrhosis**	ombitasvir/ paritaprevir/ ritonavir (o/p/r); dasabuvir (das) (Viekira Pak®)	12.5 mg/ 75 mg/ 50 mg tablets + 250 mg tablet	2 o/p/r tablets in the morning and 1 das tablet twice daily	**ribavirin**
Chronic HCV infection genotype **1b with or without compensated cirrhosis (Child-Pugh A)**			2 o/p/r tablets in the morning and 1 das tablet twice daily	**---**
Chronic HCV infection genotype 1-6 **treatment-naïve with or without compensated cirrhosis (Child-Pugh A)**	sofosbuvir/ velpatasvir (Epclusa®)	400 mg/ 100 mg tablet	One tablet once daily	**---**
Chronic HCV infection genotype 1-6 **treatment-naïve** with decompensated cirrhosis (Child-Pugh B or C)			One tablet once daily	**ribavirin**

HCV = hepatitis C virus

Table 3. DAAs for Treatment of Adult Chronic HCV Infection – Therapy for Treatment-Experienced Patients - Monotherapy

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 2 or 3 without or with compensated cirrhosis (Child-Pugh A) who have failed PegIFN/RBV	sofosbuvir (Sovaldi®)	400 mg tablets	One tablet once daily	daclatasvir

HCV = hepatitis C virus; PegIFN/RBV = pegylated interferon alfa/ ribavirin

Table 4. DAAs for Treatment of Adult Chronic HCV Infection – Therapy for Treatment-Experienced Patients – Combination Therapy

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1a (no baseline NS5A polymorphisms) or 1b who have failed PegIFN/RBV with or without cirrhosis	elbasvir/ grazoprevir (Zepatier®)	50 mg/ 100 mg tablets	One tablet once daily	---
Chronic HCV infection genotype 1a or 1b who have failed PegIFN/RBV + NS3/4A protease inhibitor or genotype 4 who have failed PegIFN/ RBV with or without cirrhosis			One tablet once daily	ribavirin

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1 without cirrhosis or with compensated cirrhosis (Child-Pugh A) previously treated with HCV NS5A inhibitor or NS3/4A protease inhibitor	glecaprevir/ pibrentasvir (Mavyret™)	100 mg/ 40 mg tablets	3 tablets with food once daily	---
Chronic HCV infection genotype 1-6 treatment-experienced patients with or without cirrhosis who have received interferon products, ribavirin, or sofosbuvir but not an NS3/4A protease inhibitor or NS5A inhibitor			3 tablets with food once daily	---
Chronic HCV infection genotype 1, 4, 5, or 6 without cirrhosis or with decompensated cirrhosis (Child-Pugh A) who have failed PegIFN/RBV with or without a protease inhibitor	ledipasvir/ sofosbuvir (Harvoni®, generics)	90 mg/ 400 mg tablets	One tablet once daily	---
Chronic HCV infection genotype 1 with decompensated cirrhosis (Child-Pugh B or C) who have failed PegIFN/RBV with or without a protease inhibitor			One tablet once daily	ribavirin

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1-6 with or without compensated cirrhosis (Child-Pugh A) who have failed PegIFN/RBV with or without an NS3/4A protease inhibitor	**sofosbuvir/ velpatasvir (Epclusa®)**	**400 mg/ 100 mg tablet**	**One tablet once daily**	**---**
Chronic HCV infection genotype 1-6 with decompensated cirrhosis (Child-Pugh B or C) who have failed PegIFN/RBV with or without an NS3/4A protease inhibitor			**One tablet once daily**	**ribavirin**
Chronic HCV infection genotype 1-6 with compensated cirrhosis (Child-Pugh A) who have previously been on an HCV regimen containing an NS5A inhibitor	sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)	400 mg/ 100 mg/ 100 mg tablet	One tablet once daily with food	**---**
Chronic HCV infection genotype 1a or 3 without cirrhosis who have previously been on an HCV regimen containing sofosbuvir without an NS5A inhibitor	sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)	400 mg/ 100 mg/ 100 mg tablet	One tablet once daily with food	**---**
Chronic HCV infection genotype 1a with compensated cirrhosis (Child-Pugh A) who have previously been on an HCV regimen containing sofosbuvir without an NS5A inhibitor			**One tablet once daily with food**	**---**

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 3 with compensated cirrhosis (Child-Pugh A) who have previously been on an HCV regimen containing sofosbuvir without an NS5A inhibitor			**One tablet once daily with food**	**ribavirin**

HCV = hepatitis C virus; NS5A inhibitors = Nonstructural protein 5A (NS5A) inhibitors; PegIFN/RBV = pegylated interferon alfa/ ribavirin

1.2 Pediatrics

Safety and efficacy of DAAs for use in children younger than 18 years of age has only been established with sofosbuvir (Sovaldi®) and ledipasvir/ sofosbuvir (Harvoni®). Recommended DAA dosages in pediatric patients are summarized in **Tables 5 and 6**.

Table 5. Maximum Recommended DAA Dosages in Pediatric Chronic HCV Infections - Monotherapy

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 2 and 3 treatment-naïve with or without compensated cirrhosis (Child-Pugh A) in patient >12 years of age or weighing >35 kg	sofosbuvir (Sovaldi®)	**400 mg tablet**	**One tablet once daily**	**ribavirin**

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 2 and 3 with or without compensated cirrhosis (Child-Pugh A) who have failed interferon regimen +/- ribavirin in patients >12 years of age or weighing >35 kg	sofosbuvir (Sovaldi®)	**400 mg tablet**	**One tablet once daily**	**ribavirin**

HCV = hepatitis C virus

Table 6. Maximum Recommended DAA Dosages in Pediatric Chronic HCV Infections – Combination Therapy

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1-6 with or without compensated cirrhosis (Child-Pugh A) in patients >12 years of age weighing ≥45 kg	**glecaprevir/ pibrentasvir (Mavyret™)**	**100 mg/ 40 mg tablets**	**3 tablets taken at same time each day with food**	**--**
Chronic HCV infection genotype 1 previously treated with NS5A inhibitor or NS3/4A protease inhibitor regimen, but not both in patients >12 years of age weighing ≥45 kg	**glecaprevir/ pibrentasvir (Mavyret™)**	**100 mg/ 40 mg tablets**	**3 tablets taken at same time each day with food**	**--**

Treatment Indication	Drug Name	Dosage Form / Strength	Maximum Recommended Dosage	Adjunctive Therapy
Chronic HCV infection genotype 1, 2, 3, 4, 5, or 6 treatment-experienced patients >12 years of age weighing ≥45 kg with or without cirrhosis who have received interferon products, ribavirin, or sofosbuvir but not an NS3/4A protease inhibitor or NS5A inhibitor			**3 tablets taken at same time each day with food**	**--**
Chronic HCV infection genotype 1, 4, 5, or 6 with or without compensated cirrhosis (Child-Pugh A) >12 years of age or weighing >35 kg	ledipasvir/ sofosbuvir (Harvoni®, **generics**)	**90 mg/ 400 mg tablet**	**One tablet once daily**	**---**

HCV = hepatitis C virus

2 Duration of Therapy[1-14]

Duration of therapy with hepatitis C DAAs is dependent on cirrhosis status, previous therapy, and hepatitis C virus genotype, with FDA-indicated treatment durations dependent on these factors. The goal of therapy is a sustained virologic response, defined as having non-detectable HCV RNA at 12 weeks post completion of DAA course. **DAA therapy duration based on genotype for adults is summarized in Tables 7-11, and is summarized for pediatric patients in Table 12.**

Table 7. Duration of DAA Therapy for HCV Genotypes 1, 1a, and 1b

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
daclatasvir (Daklinza®)	Without or compensated (Child-Pugh A)	Naïve/experienced[a]	12 weeks	sofosbuvir

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
daclatasvir (Daklinza®)	With decompensated (Child-Pugh B or C) or post liver transplant	Naïve/experienced	12 weeks	sofosbuvir and ribavirin
elbasvir/ grazoprevir (Zepatier®)[b]	Without or compensated (Child-Pugh A)	Naïve/experienced (No history of HCV protease inhibitor)	12 or 16 weeks[c]	±ribavirin[c]
elbasvir/ grazoprevir (Zepatier®)[b,d]	Without or compensated (Child-Pugh A)	Experienced with HCV protease inhibitor (e.g., boceprevir, simeprevir)	12 weeks	ribavirin
glecaprevir/ pibrentasvir (Mavyret™)	Without	Naïve	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	Naïve	12 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without or compensated (Child-Pugh A)	Prior treatment with an NS5A inhibitor containing regimen without an NS3/4A protease inhibitor	16 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without or compensated (Child-Pugh A)	Prior treatment with an NS3/4A protease inhibitor containing regimen without an NS5A inhibitor	12 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without	PEG-INF[e], ribavirin, sofosbuvir	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	PEG-INF, ribavirin, sofosbuvir	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	Without or compensated (Child-Pugh A)	Naïve	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	Without	Experienced	12 weeks	N/A

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
ledipasvir/ sofosbuvir (Harvoni®)	With compensated (Child-Pugh A)	Experienced	24 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	With decompensated (Child-Pugh B OR C)	Naïve/experienced	12 weeks	ribavirin
ledipasvir/ sofosbuvir (Harvoni®)	Post-liver transplant Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	ribavirin
ombitasvir/ paritaprevir/ ritonavir tablets and dasabuvir tablets (Viekira Pak®)[b]	Genotype 1a without	Naïve/experienced	12 weeks	ribavirin
ombitasvir/ paritaprevir/ ritonavir tablets and dasabuvir tablets (Viekira Pak®)[b]	Genotype 1a with compensated (Child-Pugh A)	Naïve/experienced	24 weeks	ribavirin
ombitasvir/ paritaprevir/ ritonavir tablets and dasabuvir tablets (Viekira Pak®)[c]	Genotype 1b without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Naïve	12 weeks	ribavirin and PEG-INF
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Previous intolerance to PEG-INF	24 weeks	ribavirin
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)	Without or compensated (Child-Pugh A)	NS5A inhibitor (e.g., daclatasvir, elbasvir)	12 weeks	N/A
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)[a]	Without or compensated (Child-Pugh A)	sofosbuvir and no NS5A	12 weeks	N/A

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
sofosbuvir/ velpatasvir (Epclusa®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A
sofosbuvir/ velpatasvir (Epclusa®)	With decompensated (Child-Pugh B OR C)	Naïve/experienced	12 weeks	ribavirin

HCV = hepatitis C virus; NS5A inhibitors = Nonstructural protein 5A (NS5A) inhibitors
[a] Treatment-experienced patients included those who have failed a peg-interferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor
[b] Genotype 1a
[c] Patients without baseline NS5A resistance polymorphisms (polymorphisms at amino acid positions 28, 30, 31, or 93) should receive 12 weeks of therapy without ribavirin; patients that have the polymorphisms should receive 16 weeks of therapy and ribavirin
[d] Genotype 1b
[e] Pegylated interferon-alfa
[f] Prior-relapser: undetectable HCV RNA at the end of prior interferon-based therapy and detectable HCV RNA during follow-up.
[g] simeprevir for 12 weeks with ribavirin and PEG-INF followed by an additional 12 weeks of ribavirin and PEG-INF alone resulting in 24 weeks for total length of therapy
[h] simeprevir for 12 weeks with ribavirin and PEG-INF followed by an additional 36 weeks of ribavirin and PEG-INF alone resulting in 48 weeks for total length of therapy
[i] Non-responder includes partial and null non-responders.
-Partial: prior on-treatment at least 2 $\log_{10}$ units/mL reduction in HCV RNA from baseline at week 12 and detectable HCV RNA at end of prior interferon-based therapy.
-Null: prior on-treatment less than 2 $\log_{10}$ reduction in HCV RNA from baseline at week 12 during prior interferon-based therapy

Table 8. Duration of DAA Therapy for HCV Genotype 2

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
glecaprevir/ pibrentasvir (Mavyret™)	Without	Naïve	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	Naïve	12 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without	PEG-INF[a], ribavirin, sofosbuvir	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	PEG-INF, ribavirin, sofosbuvir	12 weeks	N/A
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Naïve/experienced[b]	12 weeks	ribavirin

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
sofosbuvir/velpatasvir/ voxilaprevir (Vosevi®)	Without or compensated (Child-Pugh A)	NS5A inhibitor (daclatasvir, elbasvir, etc.)	12 weeks	N/A
sofosbuvir/velpatasvir (Epclusa®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A
sofosbuvir/velpatasvir (Epclusa®)	With decompensated (Child-Pugh B OR C)	Naïve/experienced	12 weeks	ribavirin

HCV = hepatitis C virus; NS5A inhibitors = Nonstructural protein 5A (NS5A) inhibitor

[a]Pegylated-interferon alfa

[b] Treatment-experienced patients included those who have failed a peg-interferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor

Table 9. Duration of DAA Therapy for HCV Genotype 3

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
daclatasvir (Daklinza®)	Without	Naïve/experienced[a]	12 weeks	sofosbuvir
daclatasvir (Daklinza®)	With compensated (Child-Pugh A) or decompensated (Child-Pugh B or C) or post liver transplant	Naïve/experienced	12 weeks	sofosbuvir and ribavirin
glecaprevir/ pibrentasvir (Mavyret™)	Without	Naïve	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	Naïve	12 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without or compensated (Child-Pugh A)	PEG-INF[b], ribavirin, sofosbuvir	16 weeks	N/A
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Naïve/experienced	24 weeks	ribavirin
sofosbuvir/velpatasvir (Epclusa®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
sofosbuvir/velpatasvir (Epclusa®)	With decompensated (Child-Pugh B OR C)	Naïve/experienced	12 weeks	ribavirin
sofosbuvir/velpatasvir/ voxilaprevir (Vosevi®)	Without or compensated (Child-Pugh A)	sofosbuvir and no NS5A inhibitor	12 weeks	N/A

[a] Treatment-experienced patients included those who have failed a peg-interferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor

[b] Pegylated-interferon alfa

Table 10. Duration of DAA Therapy for HCV Genotype 4

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
elbasvir/ grazoprevir (Zepatier®)	Without or compensated (Child-Pugh A)	Naïve	12 weeks	N/A
elbasvir/ grazoprevir (Zepatier®)	Without or compensated (Child-Pugh A)	PEG-INF[a]	16 weeks	ribavirin
glecaprevir/ pibrentasvir (Mavyret™)	Without	Naïve	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	Naïve	12 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without	PEG-INF, ribavirin, sofosbuvir	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	PEG-INF, ribavirin, sofosbuvir	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	Without or compensated (Child-Pugh A)	Naïve/experienced[b]	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	Post-liver transplant without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	ribavirin
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Naïve	12 weeks	ribavirin and PEG-INF

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)	Without or compensated (Child-Pugh A)	NS5A inhibitor (daclatasvir, elbasvir, etc.)	12 weeks	N/A
sofosbuvir/ velpatasvir (Epclusa®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A
sofosbuvir/ velpatasvir (Epclusa®)	With decompensated (Child-Pugh B OR C)	Naïve/experienced	12 weeks	ribavirin

[a] Pegylated-interferon alfa

[b] Treatment-experienced patients included those who have failed a peg-interferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor

[c] Prior-relapser: undetectable HCV RNA at the end of prior interferon-based therapy and detectable HCV RNA during follow-up

[d] simeprevir for 12 weeks with ribavirin and PEG-INF followed by an additional 12 weeks of ribavirin and PEG-INF alone resulting in 24 weeks for total length of therapy

[e] simeprevir for 12 weeks with ribavirin and PEG-INF followed by an additional 36 weeks of ribavirin and PEG-INF alone resulting in 48 weeks for total length of therapy

[f] Non-responder includes partial and null non-responders.
-Partial: prior on-treatment at least 2 $\log_{10}$ units/mL reduction in HCV RNA from baseline at week 12 and detectable HCV RNA at end of prior interferon-based therapy
-Null: prior on-treatment less than 2 $\log_{10}$ reduction in HCV RNA from baseline at week 12 during prior interferon-based therapy

Table 11. Duration of DAA Therapy for HCV Genotype 5 and 6

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
glecaprevir/ pibrentasvir (Mavyret™)	Without	Naïve	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	Naïve	12 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	Without	PEG-INF[a], ribavirin, sofosbuvir	8 weeks	N/A
glecaprevir/ pibrentasvir (Mavyret™)	With compensated (Child-Pugh A)	PEG-INF, ribavirin, sofosbuvir	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	Without or compensated (Child-Pugh A)	Naïve/experienced[b]	12 weeks	N/A

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)	Without or compensated (Child-Pugh A)	NS5A inhibitor[c] (e.g., daclatasvir, elbasvir)	12 weeks	N/A
sofosbuvir/ velpatasvir (Epclusa®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A
sofosbuvir/ velpatasvir (Epclusa®)	With decompensated (Child-Pugh B OR C)	Naïve/experienced	12 weeks	ribavirin

[a] Pegylated-interferon alfa

[b] Treatment-experienced patients included those who have failed a peg-interferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor

[c] NS5A inhibitors = Nonstructural protein 5A (NS5A) inhibitors

Table 12. Duration of DAA Therapy for Pediatric Patients

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
		Genotype 1		
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**Naïve**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**Naïve**	**12 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**Without or compensated (Child-Pugh A)**	**Prior treatment with an NS5A inhibitor containing regimen without an NS3/4A protease inhibitor**	**16 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**Without or compensated (Child-Pugh A)**	**Prior treatment with an NS3/4A protease inhibitor containing regimen without an NS5A inhibitor**	**12 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**PEG-INF[e], ribavirin, sofosbuvir**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**PEG-INF, ribavirin, sofosbuvir**	**12 weeks**	**N/A**

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
ledipasvir/ sofosbuvir (Harvoni®)	Without or compensated (Child-Pugh A)	Naïve	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	Without	Experienced[a]	12 weeks	N/A
ledipasvir/ sofosbuvir (Harvoni®)	With compensated (Child-Pugh A)	Experienced	24 weeks	N/A
		Genotype 2		
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	ribavirin
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**Naïve**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**Naïve**	**12 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**PEG-INF[a], ribavirin, sofosbuvir**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**PEG-INF, ribavirin, sofosbuvir**	**12 weeks**	**N/A**
		Genotype 3		
sofosbuvir (Sovaldi®)	Without or compensated (Child-Pugh A)	Naïve/experienced	24 weeks	ribavirin
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**Naïve**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**Naïve**	**12 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**Without or compensated (Child-Pugh A)**	**PEG-INF[b], ribavirin, sofosbuvir**	**16 weeks**	**N/A**
		Genotype 4, 5, and 6		

Drug Name	Cirrhosis	Previous Therapy	Duration	In combination with
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**Naïve**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**Naïve**	**12 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**Without**	**PEG-INF[a], ribavirin, sofosbuvir**	**8 weeks**	**N/A**
glecaprevir/ pibrentasvir (Mavyret™)	**With compensated (Child-Pugh A)**	**PEG-INF, ribavirin, sofosbuvir**	**12 weeks**	**N/A**
ledipasvir/ sofosbuvir (Harvoni®)	Without or compensated (Child-Pugh A)	Naïve/experienced	12 weeks	N/A

[a] Treatment-experienced patients included those who have failed a peg-interferon alfa plus ribavirin based regimen with or without an HCV protease inhibitor

3 Duplicative Therapy[1-14]

There are no FDA indications for duplicate therapy with multiple combination drug products (e.g., ledipasvir/ sofosbuvir (Harvoni®) with glecaprevir/ pibrentasvir (Mavyret™), as there is increased risk for adverse events without additional efficacy benefit.

Patients receiving daclatasvir require the addition of sofosbuvir to prevent potential resistance from monotherapy. Ribavirin combination therapy is also indicated in patients with more advanced liver disease and HCV genotypes that are found to be more resistant (e.g. genotype 1a).

For recommended combination therapies, see Duration of Therapy tables above **(Tables 7-12).**

4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. The following drug-drug interactions in **Table 13** are considered clinically relevant for DAAs. Only those drug-drug

interactions classified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed.

Table 13. DAA Drug-Drug Interactions

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level
daclatasvir	strong CYP3A4 inducers (e.g. phenytoin, carbamazepine, St John's wort, phenobarbital)	concurrent use may decrease plasma daclatasvir concentrations	adjunctive use contraindicated	1-severe (CP*), contraindicated (DrugReax)
daclatasvir	moderate CYP3A4 inducers (e.g., bosentan, efavirenz, etravirine, modafinil, nevirapine)	concurrent use may decrease plasma daclatasvir concentrations	adjust daclatasvir to 90 mg daily	1-severe (CP), contraindicated (DrugReax)
daclatasvir	Strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole)	Concurrent use may increase plasma daclatasvir concentrations.	Adjust daclatasvir to 30 mg daily	1-severe (CP), contraindicated (DrugReax)
dasabuvir/ ombitasvir/ paritaprevir/ ritonavir	CYP3A4 substrates/inhibitors/inducers (e.g. phenytoin, rifampin, voriconazole)	Strong CYP3A4 inhibitor and substrate	Coadministration is contraindicated	1-severe (CP), contraindicated (DrugReax)
dasabuvir/ ombitasvir/ paritaprevir/ ritonavir	QTc prolonging agents (e.g. quinidine, ziprasidone, amiodarone)	ritonavir component increases risk of QTc prolongation	Use should be avoided with other QT prolonging agents	1-severe (CP), contraindicated/ major (DrugReax)
dasabuvir/ ombitasvir/ paritaprevir/ ritonavir	ethinyl estradiol	Concurrent use may cause LFT elevation	Use is contraindicated; alternative method of contraception should be used	1-severe (CP), contraindicated (DrugReax)
dasabuvir/ ombitasvir/ paritaprevir/ ritonavir	sildenafil	ritonavir component acts as a PDE-5 inhibitor causing marked sildenafil plasma concentration elevation	Use lower sildenafil	2-major (CP), contraindicated/ major (DrugReax)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level
elbasvir	Strong CYP3A4 inducers (e.g. phenytoin, carbamazepine, St John's wort, phenobarbital)	Concurrent use may decrease elbasvir plasma concentration	Use is contraindicated	1-severe (CP), contraindicated (DrugReax)
glecaprevir/ pibrentasvir	Strong or moderate dual CYP3A4 and p-glycoprotein inducers (e.g. rifampin, isoniazid)	Concurrent use may decrease voxilaprevir plasma concentration	Coadministration should be avoided	1-severe (CP), major (DrugReax)
grazoprevir	OTAP1B1/3 inhibitors (e.g. cyclosporine, eltrombopag)	Concurrent use can increase grazoprevir concentrations and elevate ALT.	Use is contraindicated	1-severe (CP), contraindicated (DrugReax)
grazoprevir	Protease inhibitors (e.g. saquinavir, ritonavir, darunavir)	Concurrent use can increase grazoprevir concentrations and elevate ALT.	Use is contraindicated	1-severe (CP), contraindicated (DrugReax)
ledipasvir	Proton pump inhibitors (PPIs) and histamine 2 receptor antagonists (H2RAs) (e.g. omeprazole, ranitidine)	Increased pH in stomach reduces ledipasvir solubility	Use cautiously; take H2RA simultaneously or 12 hours apart from ledipasvir; PPI dose should not exceed equivalent of omeprazole 20 mg/ day. H2RA should not exceed equivalent of famotidine 40 mg/ day	2-Major (CP), Major (DrugReax)
ledipasvir	p-glycoprotein inducers (e.g. rifampin, St John's wort)	Concurrent use can decrease ledipasvir concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary.	2-Major (CP), Major (DrugReax)
simeprevir	ledipasvir	Concurrent use increases ledipasvir exposure by 92% and simeprevir exposure by 116%	Avoid coadministration	2-Major (CP), Major (DrugReax)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level
simeprevir	CYP3A4 inhibitors (e.g. ritonavir, fluconazole, erythromycin)	Concurrent use increases simeprevir concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary	2-Major (CP), Major (DrugReax)
simeprevir	CYP3A4 inducers (e.g. carbamazepine, phenytoin)	Concurrent use decreases simeprevir concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary	2-Major (CP), Major (DrugReax)
simeprevir	CYP3A4 substrates (e.g. amitriptyline, sertraline, atorvastatin)	Concurrent use increases CYP3A4 substrate concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary	2-Major (CP), Major (DrugReax)
simeprevir	p-glycoprotein inhibitors (e.g. ritonavir, fluconazole, erythromycin)	Concurrent use increases simeprevir concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary	2-Major (CP), Major (DrugReax)
simeprevir	p-glycoprotein inducers (e.g. carbamazepine, phenytoin)	Concurrent use decreases simeprevir concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary	2-Major (CP), Major (DrugReax)
simeprevir	p-glycoprotein substrates (e.g. amitriptyline, sertraline, atorvastatin)	Concurrent use increases p-glycoprotein substrate concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary	2-Major (CP), Major (DrugReax)
simeprevir	OATP1B/3 substrates (e.g. methotrexate, valsartan, glyburide)	Concurrent use increases OATP1B/3 substrate concentrations	Monitor therapeutic concentrations and make dose adjustments as necessary.	2-Major (CP), Major (DrugReax)
sofosbuvir	rifampin	Concurrent use can decrease sofosbuvir concentrations	Avoid coadministration; contraindicated	2-Major (CP), contraindicated (DrugReax)
sofosbuvir	p-glycoprotein inducers (oxcarbazepine, phenytoin)	Concurrent use can decrease sofosbuvir concentrations	Avoid coadministration	2-Major (CP), Major (DrugReax)
sofosbuvir	amiodarone	Concurrent use may increase severe bradycardia risk	Avoid coadministration	2-Major (CP), Major (DrugReax)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level
velpatasvir	Strong or moderate dual CYP3A4 and CYP2B6 inducers (e.g., primidone, phenobarbital)	Concurrent use can decrease velpatasvir concentrations	Avoid coadministration	2-major (CP), major (DrugReax)
velpatasvir	PPIs and H2RAs (e.g. omeprazole, ranitidine)	Increased pH in stomach reduces velpatasvir solubility	Use cautiously; take H2RA simultaneously or 12 hours apart from velpatasvir; PPI dose should not exceed equivalent of omeprazole 20 mg/ day; H2RA should not exceed equivalent of famotidine 40 mg/ day	2-Major (CP), Major (DrugReax)
voxilaprevir	Strong or moderate dual CYP3A4 and CYP2B6 inducers (e.g. primidone, phenobarbital)	Concurrent use can decrease voxilaprevir concentrations	Avoid coadministration	2-major (CP), major (DrugReax)
voxilaprevir	Strong or moderate dual CYP3A4 and p-glycoprotein inducers (e.g. phenytoin, St. John's wort)	Concurrent use can decrease voxilaprevir concentrations	Avoid coadministration	2-major (CP), major (DrugReax)
voxilaprevir	cyclosporine	Concurrent use can increase voxilaprevir concentrations	Avoid coadministration	2-major (CP), major (DrugReax)

**CP= Clinical Pharmacology*

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