Patients With HIV/HCV Coinfection

Recommendations Related to HCV Medication Interactions With HIV Antiretroviral Medications

RECOMMENDED	RATING
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.	I, A
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) Elbasvir/grazoprevir should be used with antiretroviral drugs with which it does not have clinically significant interactions: abacavir, bictegravir, cabotegravir, dolutegravir, doravirine, emtricitabine, ibalizumab-uiyk, lamivudine, maraviroc, raltegravir, rilpivirine, and tenofovir.	IIa, B
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a] Glecaprevir/pibrentasvir should be used with antiretroviral drugs with which it does not have clinically significant interactions: abacavir, bictegravir, cabotegravir, dolutegravir, doravirine, emtricitabine, fostemsavir, ibalizumab-uiyk, lamivudine, maraviroc, raltegravir, rilpivirine, and tenofovir. Given the increase in glecaprevir exposures and limited data on the safety of elvitegravir/cobicistat with glecaprevir/pibrentasvir, monitoring for hepatic toxicity is recommended until additional safety data are available in HIV/HCV-coinfected patients.	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) Sofosbuvir/velpatasvir can be used with most antiretrovirals but not efavirenz, etravirine, or nevirapine. Because tenofovir levels, when given as tenofovir disoproxil fumarate, may increase with sofosbuvir/velpatasvir, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR <60 mL/min. Due to limited experience with this drug combination, renal monitoring is recommended in patients taking tenofovir disoproxil fumarate and cobicistat or ritonavir with sofosbuvir/velpatasvir. Tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during sofosbuvir/velpatasvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy.	IIa, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) Ledipasvir/sofosbuvir can be used with most antiretrovirals. Because this therapy increases tenofovir levels when given as tenofovir disoproxil fumarate, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR <60 mL/min. Absolute tenofovir levels are highest and may exceed exposures for which there are established renal safety data when tenofovir disoproxil fumarate is administered with ritonavir- or cobicistat-containing regimens. Due to lack of sufficient safety data with this drug combination, consideration should be given to changing the antiretroviral regimen. If the combination is used, renal monitoring is recommended during the dosing period. Tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during ledipasvir/sofosbuvir treatment for patients taking cobicistat or ritonavir as	IIa, C

Recommendations Related to HCV Medication Interactions With HIV Antiretroviral Medications

part of their antiretroviral therapy.	
For combinations including tenofovir disoproxil fumarate wherein increased tenofovir levels are expected, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended.	IIa, C
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) Sofosbuvir/velpatasvir/voxilaprevir should be used with antiretroviral drugs with which they do not have substantial interactions: abacavir, bictegravir, cabotegravir, dolutegravir, doravirine, emtricitabine, ibalizumab-uiyk, lamivudine, maraviroc, raltegravir, rilpivirine, and tenofovir alafenamide. Given increases in voxilaprevir AUC with darunavir/ritonavir or elvitegravir/cobicistat coadministration and lack of clinical safety data, monitoring for hepatic toxicity is recommended until additional safety data are available in HIV/HCV-coinfected patients. Because this therapy has the potential to increase tenofovir levels when given as tenofovir disoproxil fumarate, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR <60 mL/min. In patients concomitantly receiving sofosbuvir/velpatasvir/voxilaprevir and tenofovir disoproxil fumarate, renal monitoring is recommended during the dosing period.	IIa, B

[a] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Regimens Not Recommended for Patients with HIV/HCV Coinfection

NOT RECOMMENDED	RATING
Antiretroviral treatment interruption to allow HCV therapy is **not** recommended.	III, A
Elbasvir/grazoprevir should **not** be used with cobicistat, efavirenz, etravirine, nevirapine, or any HIV protease inhibitor.	III, B
Glecaprevir/pibrentasvir should **not** be used with atazanavir, efavirenz, etravirine, nevirapine, or ritonavir-containing antiretroviral regimens.	III, B
Sofosbuvir/velpatasvir should **not** be used with efavirenz, etravirine, or nevirapine.	III, B
Sofosbuvir/velpatasvir/voxilaprevir should **not** be used with efavirenz, etravirine, nevirapine, ritonavir-boosted atazanavir, or ritonavir-boosted lopinavir.	III, B
Sofosbuvir-based regimens should **not** be used with tipranavir.	III, B
Ribavirin should **not** be used with didanosine, stavudine, or zidovudine.	III, B

Table. Drug Interactions Between Direct-Acting Antivirals and Antiretroviral Drugs—Recommended Regimens

		Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
Protease Inhibitors	**Boosted Atazanavir**	A	A			
	Boosted Darunavir	A	A			
	Boosted Lopinavir	ND, A	A			ND
NNRTIs	**Doravirine**		ND		ND	ND
	Efavirenz				ND	ND
	Rilpivirine					
	Etravirine	ND	ND	ND	ND	ND
Integrase Inhibitors	**Bictegravir**			ND	ND	
	Cabotegravir	ND	ND	ND	ND	ND
	Cobicistat-boosted elvitegravir	C	C			C
	Dolutegravir					ND
	Raltegravir					ND
Entry Inhibitors	**Fostemsavir**	ND	ND	ND	ND	ND
	Ibalizumab-uiyk	ND	ND	ND	ND	ND
	Maraviroc	ND	ND	ND	ND	ND
NRTIs	**Abacavir**		ND	ND		ND
	Emtricitabine					
	Lamivudine		ND	ND		ND
	Tenofovir disoproxil fumarate	B, C	B, C			C
	Tenofovir alafenamide	D	D	ND		D

Green indicates coadministration is safe; yellow indicates a dose change or additional monitoring is warranted; and red indicates the combination should be avoided.

ND: No data
A: Caution only with tenofovir disoproxil fumarate
B: Increase in tenofovir depends on which additional concomitant antiretroviral agents are administered.
C: Avoid tenofovir disoproxil fumarate in patients with an eGFR <60 mL/min; tenofovir concentrations may exceed those with established renal safety data in individuals on ritonavir- or cobicistat-containing regimens.
D: Studied as part of fixed-dose combinations with ledipasvir/sofosbuvir or sofosbuvir/velpatasvir plus TAF, emtricitabine, elvitegravir, and cobicistat.

		Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
For antiretroviral agents not included in the table above, please refer to the US Department of Health and Human Services HIV treatment guidelines (https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines) and/or the University of Liverpool drug interactions website (www.hep-druginteractions.org).						

Treatment Recommendations for Patients With HIV/HCV Coinfection	
RECOMMENDED	RATING
HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed).	I, B

Last update: October 24, 2022

Patients With Decompensated Cirrhosis

Recommended for All Patients With HCV Infection Who Have Decompensated Cirrhosis	
RECOMMENDED	RATING
Patients with HCV infection who have decompensated cirrhosis—moderate or severe hepatic impairment, ie, Child-Turcotte-Pugh (CTP) class B or class C—should be referred to a medical practitioner with expertise in that condition, ideally in a liver transplant center.	I, C

Decompensated Cirrhosis Genotype 1-6

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1-6 and Are Ribavirin Eligible

RECOMMENDED	DURATION	RATING
Genotype 1-6: Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[b]	12 weeks	I, A[c]
Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated to weight-based dose)	12 weeks	I, A[d]

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma.
[b] Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis; increase as tolerated.
[c] Only available data for genotype 6 are in patients with compensated cirrhosis.
[d] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1-6 and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Genotype 1-6: Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A[b]
Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	24 weeks	I, A[c]

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma.
[b] Only available data for genotype 6 are in patients with compensated cirrhosis.
[c] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] and Genotype 1-6 Infection in Whom Prior Sofosbuvir- or NS5A Inhibitor-Based Treatment Failed

RECOMMENDED	DURATION	RATING
Genotype 1-6: Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[b]	24 weeks	II, C[c]
Prior sofosbuvir-based treatment failure, genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg; increase as tolerated)	24 weeks	II, C[d]

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] and Genotype 1-6 Infection in Whom Prior Sofosbuvir- or NS5A Inhibitor-Based Treatment Failed

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma.
[b] Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis.
[c] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.
[d] Only available data for genotype 6 are in patients with compensated cirrhosis.

Regimens not recommended for:

Patients With Decompensated Cirrhosis (Moderate or Severe Hepatic Impairment; Child-Turcotte-Pugh Class B or C)

NOT RECOMMENDED	RATING
Any protease inhibitor-containing regimen (eg, glecaprevir, grazoprevir, and voxilaprevir).	III, B
Interferon-based regimens	III, B

Last update: October 24, 2022

Patients Who Develop Recurrent HCV Infection Post Liver Transplantation

Post Liver Transplantation: Genotype 1-6

Recommended regimens listed by pangenotypic activity, evidence level and alphabetically for:

Treatment-Naive and -Experienced Patients With Genotype 1-6 Infection in the Allograft Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	12 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, B

Recommended regimens listed by pangenotypic activity, evidence level and alphabetically for:

Treatment-Naive and -Experienced Patients With Genotype 1-6 Infection in the Allograft Without Cirrhosis

Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, B

[a] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive and -Experienced Patients With Genotype 1-6 Infection in the Allograft With Compensated Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, B
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	12 weeks	I, C
Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A

[a] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive and -Experienced Patients With Genotype 1-6 Infection in the Allograft and Decompensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/ ribavirin starting at 600 mg and increased as tolerated[b]	12 to 24 weeks[c]	I, B
Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)[b]	12 to 24 weeks[c]	I, B

[a] Includes CTP class B and class C patients.
[b] The starting dose of ribavirin should be 600 mg/d and increased or decreased as tolerated. If renal dysfunction is present, a lower starting dose is recommended. Maximum ribavirin dose is 1000 mg/d if <75 kg and 1200 mg/d if ≥75 kg body weight.
[c] 24-week treatment duration is recommended if treatment experienced.

Recommended regimen for:

DAA-Experienced Patients With Genotype 1-6 Infection in the Allograft, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)[b]	12 weeks	I, C

[a] Excludes CTP class B and class C patients.
[b] For patients with cirrhosis plus multiple negative baseline characteristic, consideration should be given to adding ribavirin. The starting dose of ribavirin should be 600 mg/d and increased or decreased as tolerated. If renal dysfunction is present, a lower starting dose is recommended. Maximum ribavirin dose is 1000 mg/d if <75 kg and 1200 mg/d if ≥75 kg body weight.

Table. DAA Interactions With Calcineurin Inhibitors

	Cyclosporine (CSA)	Tacrolimus (TAC)
Sofosbuvir (SOF)	4.5-fold ? in SOF AUC, but GS-331007 metabolite unchanged; no a priori dose adjustment	No interaction observed; no a priori dose adjustment
Ledipasvir	No data; no a priori dose adjustment	No data; no a priori dose adjustment
Elbasvir / grazoprevir (EBR/GZR)	15-fold ? in GZR AUC and 2-fold ? in EBR AUC; combination is not recommended	43% ? in TAC; no a priori dose adjustment
Velpatasvir	No interaction observed; no a priori dose adjustment	No data; no a priori dose adjustment
Glecaprevir / pibrentasvir (GLE/PIB)	5-fold ? in GLE AUC with higher doses (400 mg) of CSA; not recommended in patients requiring stable CSA doses >100 mg/day	1.45-fold ? in TAC AUC; no a priori dose adjustment; monitor TAC levels and titrate TAC dose as needed
Sofosbuvir / velpatasvir / voxila previr (SOF/VEL/VOX)	9.4-fold ? in VOX AUC; combination is not recommended	No data; no a priori dose adjustment

AUC=area under the curve

Last update: October 24, 2022

Treatment of HCV-Uninfected Transplant Recipients Receiving Organs From HCV-Viremic Donors

Recommendations When Considering Use of HCV-Viremic Donor Organs in HCV-Uninfected Recipients

RECOMMENDED	RATING
Informed consent should include the following elements: • Risk of transmission from an HCV-viremic donor • Risk of liver disease if HCV treatment is not available or treatment is unsuccessful • Risk of graft failure • Risk of extrahepatic complications, such as HCV-associated renal disease • Risk of HCV transmission to partner • Benefits, specifically reduced waiting time and possibly lower waiting list mortality • Other unknown long-term consequences (hepatic and extrahepatic) of HCV exposure (even if cure is attained)	I, C
Transplant programs should have a programmatic strategy to: • Document informed consent • Assure access to HCV treatment and retreatment(s), as necessary • Ensure long-term follow-up of recipients (beyond SVR12)	I, C

Recommendation Regarding Timing of DAA Therapy for HCV-Negative Recipients of HCV-Viremic Liver Transplant

RECOMMENDED	RATING
Early[a] treatment with a pangenotypic DAA regimen is recommended when the patient is clinically stable.	II, B

[a] Early treatment refers to starting within the first 2 weeks after liver transplant but preferably within the first week when the patient is clinically stable.

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment of HCV-Uninfected Recipients of Liver Grafts from HCV-Viremic Donors

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, C
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, C

[a] Other considerations in selection of the DAA regimen:

- Presence of liver dysfunction (eg, elevated bilirubin) as protease inhibitors should be avoided
- Specific drugs that are contraindicated or not recommended with specific DAA agents, including but not limited to:
  - High-dose antacid therapy (eg, twice daily proton pump inhibitor)
  - Amiodarone (contraindicated with sofosbuvir-inclusive regimens; see prescribing information)
  - Specific statins (eg, atorvastatin)
- Consideration of immunosuppressive drugs and DAA interactions (see below)

[b] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Recommendation Regarding Timing of DAA Therapy for HCV-Negative Recipients of HCV-Viremic Non-Liver Solid Organ Transplant

RECOMMENDED	RATING
Prophylactic[a] or preemptive[b] treatment with a pangenotypic DAA regimen is recommended.	II, B

[a] Initiate DAA therapy immediately pretransplant or on day 0 posttransplant. No HCV RNA testing of the transplant recipient is required
[b] Initiate DAA therapy on day 0 to day 7 posttransplant, as soon as the patient is clinically stable. Demonstration of HCV viremia in the transplant recipient is not required

Recommended regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment of HCV-Uninfected Recipients of Non-Liver Organs from HCV-Viremic Donors

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, C
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, C

[a] Other considerations in selection of the DAA regimen:

- Presence of liver dysfunction (eg, elevated bilirubin) as protease inhibitors should be avoided
- Specific drugs that are contraindicated or not recommended with specific DAA agents, including but not limited to:
  - High-dose antacid therapy (eg, twice daily proton pump inhibitor)
  - Amiodarone (contraindicated with sofosbuvir-inclusive regimens; see prescribing information)
  - Specific statins (eg, atorvastatin)
- Consideration of immunosuppressive drugs and DAA interactions (see below)

[b] 8 weeks is recommended for prophylactic/preemptive treatment approaches. However, if treatment initiation is delayed beyond the first week after transplant, treatment should be continued for 12 weeks. Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Last update: December 19, 2023

Patients with Renal Impairment

Recommendation for Patients With CKD Stage[a]

RECOMMENDED	RATING
No dose adjustment in direct-acting antivirals is required when using recommended regimens.[b]	I, A or IIa, B[c]

[a] Chronic kidney disease (CKD) stages: 1 = normal (eGFR >90 mL/min); 2 = mild CKD (eGFR 60-89 mL/min); 3 = moderate CKD (eGFR 30-59 mL/min); 4 = severe CKD (eGFR 15-29 mL/min); 5 = end-stage CKD (eGFR <15 mL/min)
[b] A ribavirin dose reduction may be required for patients with CKD stage 3, 4, or 5; see prescribing information for details.
[c] The rating is I, A for patients with CKD stage 1, 2, or 3 and IIa, B for those with CKD stage 4 or 5.

Last update: October 24, 2022

Kidney Transplant Patients

Post Kidney Transplantation: Genotype 1-6

Recommended and alternative regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive and Non-DAA-Experienced Kidney Transplant Patients With Genotype 1-6 Infection, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, A[c] IIa, C[d]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	IIa, C
Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Genotype 1 or 4 only: Daily fixed-dose combination of elbasvir (50 mg)/ grazoprevir (100 mg) for patients without baseline NS5A RASs[e] for elbasvir	12 weeks	I, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.
[c] Based on evidence for patients without cirrhosis.
[d] Based on evidence for patients with compensated cirrhosis.
[e] Includes genotype 1a resistance-associated substitutions at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.

Recommended regimen for:

DAA-Experienced Kidney Transplant Patients With Genotype 1-6 Infection, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg), with or without ribavirin[b]	12 weeks	IIa, C

[a] Excludes CTP class B and class C patients. For decompensated cirrhosis, please refer to the appropriate section.
[b] For patients with cirrhosis and multiple negative baseline characteristic, consideration should be given to adding ribavirin. If renal dysfunction is present, a lower starting dose is recommended. Maximum ribavirin dose is 1000 mg/d for patients who weigh <75 kg and 1200 mg/d for those who weigh ≥75 kg.

For additional information on treatment of DAA failures post transplant, treatment of decompensated cirrhosis following transplantation, treatment of transplant recipients from HCV-positive donors, and post-transplant drug-drug interactions, please see Patients Who Develop Recurrent HCV Infection Post Liver Transplantation.

Last update: October 24, 2022

Management of Acute HCV Infection

Diagnosis of Acute HCV

Recommended Testing for Diagnosing Acute HCV Infection

RECOMMENDED	RATING
HCV antibody and HCV RNA testing are recommended when acute HCV infection is suspected due to exposure, clinical presentation, or elevated aminotransferase levels (see Testing Algorithm figure).	I, C

Pharmacologic Prophylaxis

Pharmacologic Prophylaxis Not Recommended

NOT RECOMMENDED	RATING
Pre-exposure or post-exposure prophylaxis with antiviral therapy is not recommended.	III, C

Pharmacologic Prophylaxis Not Recommended

Medical Management and Monitoring of Acute HCV Infection

Recommendations for Medical Management and Monitoring of Acute HCV Infection	
RECOMMENDED	RATING
After the initial diagnosis of acute HCV with viremia (defined as quantifiable RNA), HCV treatment should be initiated without awaiting spontaneous resolution.	I, B
Counseling is recommended for patients with acute HCV infection to avoid hepatotoxic insults, including hepatotoxic drugs (eg, acetaminophen) and alcohol consumption, and to reduce the risk of HCV transmission to others.	I, C
Referral to an addiction medicine specialist is recommended for patients with acute HCV infection related to substance use.	I, B

Antiviral Therapy

Recommended Regimens for Patients With Acute HCV Infection	
RECOMMENDED	RATING
Owing to high efficacy and safety, the same regimens that are recommended for chronic HCV infection are recommended for acute infection.	IIa, C

Last reviewed: October 24, 2022

HCV in Pregnancy

Testing

Recommendation for Universal Hepatitis C Screening in Pregnancy	
RECOMMENDED	RATING
As part of prenatal care, all pregnant persons should be tested for HCV infection with each pregnancy, ideally at the initial visit. (See Recommendations for Initial HCV Testing and Follow-Up.)	I, B

Whom to Treat

Recommendation Regarding HCV Treatment and Pregnancy	
RECOMMENDED	RATING
For women of reproductive age with known HCV infection, antiviral therapy is recommended **before** considering pregnancy, whenever practical and feasible, to reduce the risk of HCV transmission to future offspring.	I, B

Monitoring During Pregnancy

Recommendations for Monitoring HCV-Infected Women During Pregnancy	
RECOMMENDED	RATING
HCV RNA and routine liver function tests are recommended at initiation of prenatal care for HCV-antibody–positive pregnant persons to assess the risk of mother-to-child transmission (MTCT) and severity of liver disease.	I, B
All pregnant persons with HCV infection should receive prenatal and intrapartum care that is appropriate for their individual obstetric risk(s) as there is no currently known intervention to reduce MTCT.	I, B
In HCV-infected pregnant persons with pruritus or jaundice, there should be a high index of suspicion for intrahepatic cholestasis of pregnancy (ICP) with subsequent assessment of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum bile acids.	I, B
HCV-infected persons with cirrhosis should be counseled about the increased risk of adverse maternal and perinatal outcomes. Antenatal and perinatal care should be coordinated with a maternal-fetal medicine (ie, high-risk pregnancy) obstetrician.	I, B

Postpartum Issues

Recommendations Regarding Breastfeeding and Postpartum Care for HCV-Infected Women	
RECOMMENDED	RATING
Breastfeeding is not contraindicated in women with HCV infection, except when the mother has cracked, damaged, or bleeding nipples, or in the context of HIV coinfection.	I, B
Women with HCV infection should have their HCV RNA reevaluated after delivery to assess for spontaneous clearance.	I, B

Last update: December 19, 2023

HCV in Children

Testing

Recommendations for HCV Testing of Perinatally Exposed Children and Siblings of Children With HCV Infection	
RECOMMENDED	RATING
All children born to HCV-infected women should be tested for HCV infection. Testing is recommended using an antibody-based test at or after 18 months of age.	I, A
Repetitive HCV RNA testing prior to 18 months of age is not recommended.	III, A
Children who are anti-HCV positive after 18 months of age should be tested with an HCV-RNA assay after age 3 to confirm chronic hepatitis C infection.	I, A
The siblings of children with vertically-acquired chronic HCV should be tested for HCV infection, if born from the same mother.	I, C

Transmission and Prevention

Recommendations for Counseling Parents Regarding Transmission and Prevention in Children with HCV Infection	
RECOMMENDED	RATING
Parents should be informed that hepatitis C is not transmitted by casual contact and, as such, children with HCV infection do not pose a risk to other children and can participate in school, sports, and athletic activities, and engage in all other regular childhood activities without restrictions.	I, B
Parents should be informed that universal precautions should be followed at school and in the home of children with HCV infection. Educate families and children about the risk and routes of HCV transmission, and the techniques for avoiding blood exposure, such as avoiding the sharing of toothbrushes, razors, and nail clippers, and the use of gloves and dilute bleach to clean up blood.	I, B

Monitoring and Medical Management

Recommendations for Monitoring and Medical Management of Children With HCV Infection	
RECOMMENDED	RATING
Routine liver biochemistries at initial diagnosis and at least annually thereafter are recommended to assess for disease progression.	I, C
Appropriate vaccinations are recommended for children with chronic HCV infection who are not immune to hepatitis B virus and/or hepatitis A virus to prevent these infections.	I, C
Disease severity assessment via routine laboratory testing and physical examination, as well as use of evolving noninvasive modalities (ie, elastography, imaging, or serum fibrosis markers) is recommended for all children with chronic HCV infection.	I, B
Children with cirrhosis should undergo hepatocellular carcinoma (HCC) surveillance and endoscopic surveillance for varices per standard recommendations.	I, B
Hepatotoxic drugs should be used with caution in children with chronic HCV infection after assessment of potential risks versus benefits of treatment. Use of corticosteroids, cytotoxic chemotherapy, and/or therapeutic doses of acetaminophen are not contraindicated in children with chronic HCV infection.	II, C
Solid organ transplantation and bone marrow transplantation are not contraindicated in children with chronic HCV infection.	II, C
Anticipatory guidance about the potential risks of ethanol for progression of liver disease is recommended for adolescents with chronic HCV infection and their families. Abstinence from alcohol and interventions to facilitate cessation of alcohol consumption, when appropriate, are advised for all persons with chronic HCV infection.	I, C

Recommendations for Monitoring and Medical Management of Children With HCV Infection

Whom and When to Treat Among Children and Adolescents With HCV Infection

Recommendations for Whom and When to Treat Among Children and Adolescents With HCV Infection

RECOMMENDED	RATING
Direct-acting antiviral (DAA) treatment with an approved regimen is recommended for all children and adolescents with HCV infection aged ≥3 years as they will benefit from antiviral therapy, regardless of disease severity.	I, B
The presence of extrahepatic manifestations—such as cryoglobulinemia, rashes, and glomerulonephritis—as well as advanced fibrosis should lead to early antiviral therapy to minimize future morbidity and mortality.	I, C

HCV Antiviral Therapy for Children and Adolescents, Without Cirrhosis or With Compensated Cirrhosis (Child-Pugh A)

Recommended regimens listed by pangenotypic, evidence level and alphabetically for

Treatment-Naive or Interferon-Experienced Children and Adolescents Without Cirrhosis or With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Combination of glecaprevir/pibrentasvir (weight-based dosing; see Table 1) for children aged ≥ 3 with any genotype[b]	8 weeks	I, B
Combination of sofosbuvir/velpatasvir (weight-based dosing; see Table 2) for children ≥3 of age with any genotype	12 weeks	I, B
Combination of ledipasvir/sofosbuvir (weight-based dosing; see Table 3) for children aged ≥3 years with genotype 1, 4, 5, or 6	12 weeks	I, B

Recommended regimens listed by pangenotypic, evidence level and alphabetically for

Treatment-Naive or Interferon-Experienced Children and Adolescents Without Cirrhosis or With Compensated Cirrhosis[a]

[a] Child-Pugh A
[b] A longer duration of therapy (ie, 16 weeks) may be needed for genotype 3 interferon-experienced patients.

Recommended regimens listed by pangenotypic, evidence level and alphabetically for

DAA-Experienced Children and Adolescents, Without Cirrhosis or With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Genotype 1, 2, 4, 5, or 6: Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) for adolescents aged ≥12 years or weighing ≥45 kg with prior exposure to an interferon-based regimen (± ribavirin) and/or sofosbuvir but no exposure to NS3/4A or NS5A protease inhibitors, without cirrhosis	8 weeks	I, C
Genotype 1, 2, 4, 5, or 6: Combination of glecaprevir/pibrentasvir (weight-based dosing; see Table 1) with prior exposure to an interferon-based regimen (± ribavirin) and/or sofosbuvir but no exposure to NS3/4A or NS5A protease inhibitors, with compensated cirrhosis[a]	12 weeks	I, C
Genotype 3: Combination of glecaprevir/pibrentasvir (weight-based dosing; see Table 1) with prior exposure to an interferon-based regimen (± ribavirin) and/or sofosbuvir but no exposure to NS3/4A or NS5A protease inhibitors, without cirrhosis or with compensated cirrhosis[a]	16 weeks	I, C
Genotype 1- 6: Combination of glecaprevir/pibrentasvir (weight-based dosing; see Table 1) with prior exposure to NS3/4A protease inhibitors but no NS5A inhibitor exposure, without cirrhosis or with compensated cirrhosis[a]	12 weeks	I, C
Genotype 1- 6: Combination of glecaprevir/pibrentasvir (weight-based dosing; see Table 1) with prior exposure to an NS5A inhibitor but no NS3/4A protease inhibitor exposure, without cirrhosis or with compensated cirrhosis[a]	16 weeks	I, C
Genotypes 1-6: Combination of sofosbuvir/velpatasvir (weight-based dosing; see Table 2) with prior exposure to an interferon-based regimen (± ribavirin) and/or sofosbuvir but no exposure to NS3/4A or NS5A protease inhibitors, without cirrhosis or with compensated cirrhosis	12 weeks	I, C
Genotypes 1-6: Combination of sofosbuvir/velpatasvir (weight-based dosing; see	12 weeks	I, C

Recommended regimens listed by pangenotypic, evidence level and alphabetically for **DAA-Experienced Children and Adolescents, Without Cirrhosis or With Compensated Cirrhosis**[a]		
Table 2) with weight-based ribavirin (see Table 4) with prior exposure to an interferon-based regimen (± ribavirin) and/or sofosbuvir but no exposure to NS3/4A or NS5A protease inhibitors, with decompensated cirrhosis		
Genotype 4, 5, or 6: Combination of ledipasvir/sofosbuvir (weight-based dosing; see Table 3) for children and adolescents aged ≥3 years with prior exposure to an interferon (± ribavirin) plus an HCV protease inhibitor regimen, without cirrhosis or with compensated cirrhosis[a]	12 weeks	I, C
Genotype 1: Combination of ledipasvir/sofosbuvir (weight-based dosing; see Table 3) for children and adolescents aged ≥3 years with prior exposure to an interferon (± ribavirin) plus an HCV protease inhibitor regimen, without cirrhosis	12 weeks	I, C
Genotype 1: Combination of ledipasvir/sofosbuvir (weight-based dosing; see Table 3) for children and adolescents aged ≥3 years with prior exposure to an interferon (± ribavirin) plus an HCV protease inhibitor regimen, with compensated cirrhosis[a]	24 weeks	I, C
[a] Child-Pugh A		

Table 1: Weight-Based Dosing of Glecaprevir/Pibrentasvir for Children Aged ≥3 Years of Age

Body Weight	Once Daily Dose of Glecaprevir/Pibrentasvir
<20 kg	150 mg/60 mg
≥20 kg to <30 kg	200 mg/80 mg
≥30 kg to <45 kg	250 mg/100 mg
45 kg and greater or 12 years of age and older	300 mg / 120 mg / day

Table 2: Weight-based dosing for sofosbuvir/velpatasvir fixed dose combination in children ≥ 3 years of age

Body Weight	Once Daily Dose of Sofosbuvir/Velpatasvir
< 17 kg	150 mg/37.5 mg
17 - < 30 kg	200 mg/50 mg
≧ 30 kg	400 mg/100 mg

Table 3: Weight-Based Dosing of Ledipasvir/Sofosbuvir for Children Aged ≥3 Years

Body Weight	Once Daily Dose of Ledipasvir/Sofosbuvir
<17 kg	33.75 mg/150 mg
17 to <35 kg	45 mg/200 mg
≥35 kg	90 mg/400 mg per day

Table 4. Weight-Based Dosing of Ribavirin for Children Aged ≥3 Years

Body Weight	Daily Dose of Ribavirin (divided AM and PM)
<47 kg	15 mg/kg
47 to 49 kg	600 mg
50 to 65 kg	800 mg
66 to 80 kg	1000 mg
>80 kg	1200 mg

Last update: October 24, 2022

Key Populations: Identification and Management of HCV in People Who Inject Drugs

Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)	
RECOMMENDED	RATING
Annual HCV testing is recommended for PWID with no prior testing, or past negative testing and subsequent injection drug use. Depending on the level of risk, more frequent testing may be	IIa, C

Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)	
indicated.	
Substance use disorder treatment programs and needle/syringe exchange programs should offer routine, opt-out HCV-antibody testing with reflexive or immediate confirmatory HCV-RNA testing and linkage to care for those who are infected.	IIa, C
PWID should be counseled about measures to reduce the risk of HCV transmission to others.	I, C
PWID should be offered linkage to harm reduction services including intranasal naloxone, needle/syringe service programs, medications for opioid use disorder, and other substance use disorder treatment programs.	I, B
Active or recent drug use or a concern for reinfection is **not** a contraindication to HCV treatment.	IIa, B

Recommendation for Testing for Reinfection in People Who Inject Drugs (PWID)	
RECOMMENDED	RATING
At least annual HCV-RNA testing is recommended for PWID with recent injection drug use after they have spontaneously cleared HCV infection or have been successfully treated.	IIa, C

Last reviewed: December 19, 2023

HCV in Key Populations: Men Who Have Sex With Men

Testing

Recommendations for Testing and Prevention of HCV Infection in Men Who Have Sex With Men (MSM)	
RECOMMENDED	RATING
Annual HCV testing is recommended for sexually active HIV-infected adolescent and adult MSM. Depending on the presence of high-risk sexual or drug use practices, more frequent testing may be warranted.	IIa, C
HCV testing at HIV pre-exposure prophylaxis (PrEP) initiation and at least annually thereafter (while on PrEP) is recommended in HIV-uninfected MSM. Depending on sexual or drug use risk practices, more frequent testing may be warranted.	IIa, C
All MSM should be counseled about the risk of sexual HCV transmission with high-risk sexual and drug use practices, and educated about measures to prevent HCV infection or transmission.	IIa, C

Treatment

Recommendation on Treatment of HCV in Men Who Have Sex With Men (MSM)	
RECOMMENDED	RATING
Antiviral treatment for HCV-infected MSM should be coupled with ongoing counseling about the risk of HCV reinfection, and education about methods to reduce HCV reinfection risk after cure.	I, B

Testing for HCV Reinfection

Recommendation on Prevention of HCV Reinfection in Men Who Have Sex With Men (MSM)	
RECOMMENDED	RATING
At least annual (and risk-based, if indicated) HCV testing with HCV RNA is recommended for	IIa, C

Recommendation on Prevention of HCV Reinfection in Men Who Have Sex With Men (MSM)	
sexually active MSM after successful treatment or spontaneous clearance of HCV infection.	

Last reviewed: October 24, 2022