بسم الله الرحمن الرحيم

- الحمد لله رب العالمين والصلاة والسلام علي سيدنا محمد الصادق الوعد الأمين ، اللهم أخرجنا من ظلمات الجهل والوهم ، إلى نور المعرفة والعلم..

Recommendations

- The goal of therapy is to cure HCV infection, in order to: (i) prevent the complications of HCV-related liver and extra-hepatic diseases, including hepatic necro-inflammation, fibrosis, cirrhosis, decompensation of cirrhosis, HCC, severe extra-hepatic manifestations and death; (ii) improve quality of life and remove stigma; and (iii) prevent onward transmission of HCV (**A1**).
- The endpoint of therapy is undetectable HCV RNA in serum or plasma by a sensitive assay (lower limit of detection ≤15 IU/ml) 12 weeks (SVR12) or 24 weeks (SVR24) after the end of treatment (**A1**).
- Undetectable HCV core antigen in serum or plasma 24 weeks (SVR24) after the end of treatment can be used as an alternative endpoint of therapy in patients with detectable HCV core antigen prior to therapy, if HCV RNA assays are not available and/or not affordable (**A1**).
- Undetectable HCV RNA in serum or plasma 24 weeks (SVR24) after the end of treatment, using a qualitative HCV RNA assay with a lower limit of detection ≤1,000 IU/ml (3.0 Log_{10} IU/ml), can be used as an alternative endpoint of therapy in areas where sensitive HCV RNA assays are not available and/or not affordable (**B1**).
- In patients with advanced fibrosis and cirrhosis, surveil-lance for HCC must be continued because an SVR will reduce, but not abolish, the risk of HCC (**A1**).

All Patients Are Now Prioritized for Treatment including TN NC

AASLD[1] Last updated November 2017	WHO[2] Last updated April 2017	EASL[3]
Treatment is indicated for:		
All patients with chronic HCV infection, except those with short life expectancies that cannot be remediated	All adults and children with chronic HCV infection, including PWID	*All patients with HCV infection must be considered for therapy, including treatment-naïve patients and individuals who failed to achieve SVR after prior treatment (A1).*

- NC, non-cirrhotic; PWID, people who inject drugs; TN, treatment naive.

- 1. AASLD recommendations for testing, managing and treating hepatitis C. Available at: http://www.hcvguidelines.org/full-report-view (accessed January 2018);
2. WHO guidelines for the screening, care and treatment of persons with chronic HCV infection Available at: http://apps.who.int/iris/bitstrea m/10665/205035/1/9789241549615_eng.pdf?ua=1(accessed January 2018)
3. http://www.journal-of-hepatology.eu/article/S0168-8278(18)31968-8/fulltext. .

The following laboratory tests are recommended within 12 weeks prior to starting antiviral therapy: Complete blood count (CBC) International normalized ratio (INR) Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels) Calculated glomerular filtration rate (eGFR) The following laboratory tests are recommended at any time prior to starting antiviral therapy: HCV genotype and subtype Quantitative HCV RNA (HCV viral load) I, C Patients scheduled to receive an HCV NS3 protease inhibitor (ie, paritaprevir, simeprevir, grazoprevir, voxilaprevir, glecaprevir) should be assessed for a history of decompensated liver disease and for liver disease severity using the Child-Turcotte-Pugh (CTP) score (see third-party calculator). Patients with current or prior history of decompensated liver disease or with a current CTP

HCV DAAs

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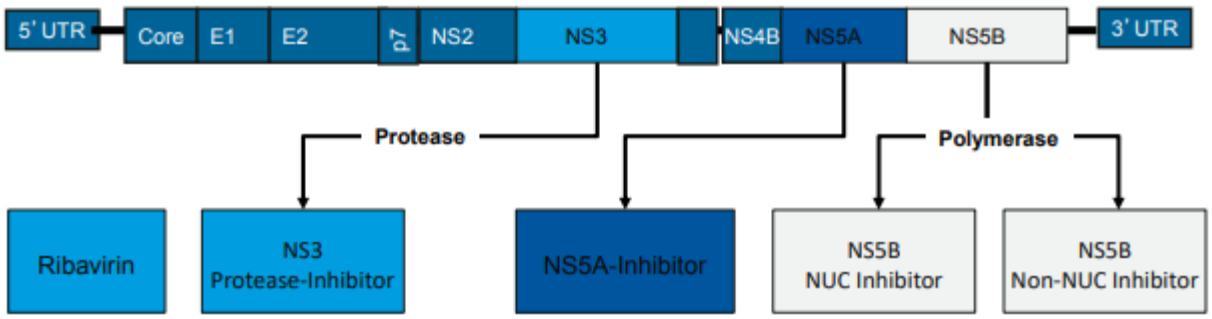

Telaprevir	Daclatasvir	Sofosbuvir	Dasabuvir
Boceprevir	Ledipasvir	VX-135	Beclabuvir
Simeprevir	Velpatasvir	IDX21437	Uprifosbuvir
Paritaprevir	Ombitasvir	ACH-3422	
Asunaprevir	Elbasvir		
Grazoprevir	Pibrentasvir		
Glecaprevir	Ruzasvir		
Voxilaprevir			
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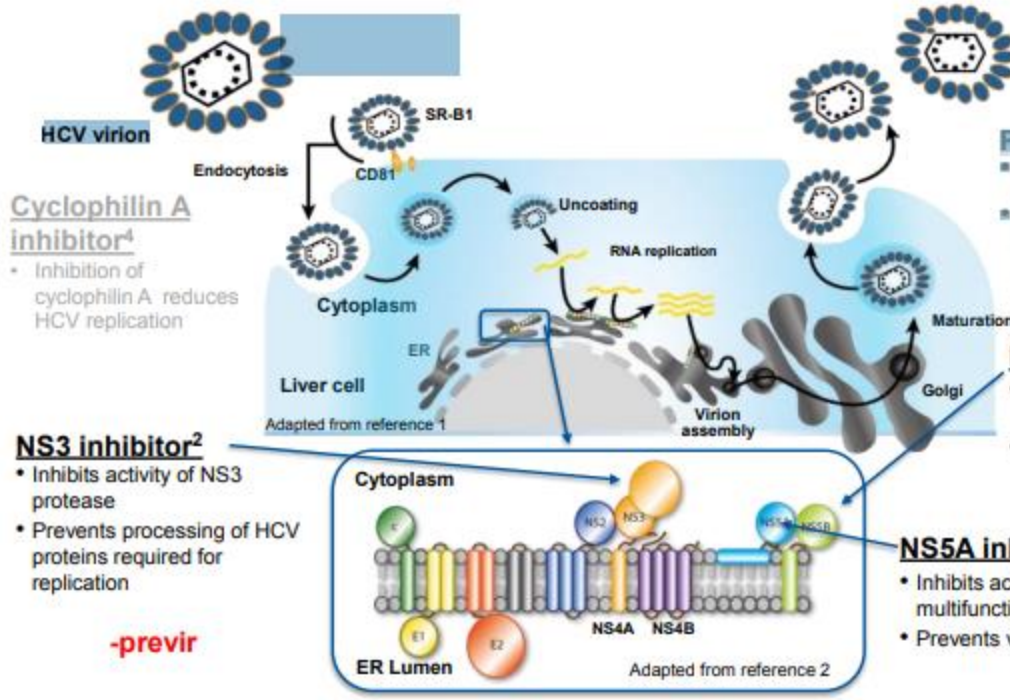

Cyclophilin A inhibitor[4]

- Inhibition of cyclophilin A reduces HCV replication

PEG-IFN lambda[3]

- Type III pegylated interferon
- Expression of receptor is more limited than Alfa, should lead to improved tolerability and safety

NS3 inhibitor[2]

- Inhibits activity of NS3 protease
- Prevents processing of HCV proteins required for replication

-previr

NS5B inhibitor(s)[2]

- Inhibits NS5B RNA replicase
- Prevents replication of viral genome

-buvir

NS5A inhibitor[2]

- Inhibits activity of NS5A, a multifunctional protein
- Prevents viral replication

-asvir

1. Manns MP, et al. Nat Rev Drug Discov 2007;6:991–1000. 2. Rice C. Top Antivir Med 2011;19(3):117–20. 3. Donnelly R, et al. Trends Immunol 2011;32(9):443–50. 4. Gallay P, Lin K. Drug Des Devel Ther 2013;7:105–15

Recommended Assessments Prior to Starting Antiviral Therapy

score ≥7 should **not** receive treatment with regimens that contain NS3 protease inhibitors due to increased blood levels and/or lack of safety data.

- Similarly, patients with a CTP score of 5 or 6 who cannot be closely monitored for laboratory or clinical symptoms during treatment should **not** receive treatment with a regimen that contains paritaprevir/ritonavir.

ll patients initiating HCV direct-acting antiviral (DAA) therapy should be assessed for HBV oinfection with HBsAg testing, and for evidence of prior infection with anti-HBs and anti-HBc testing.

esting for the presence of resistance-associated substitutions (RASs) prior to starting treatment hould be performed as recommended in the Initial Treatment and the Retreatment sections.

Quantitative HCV viral load testing is recommended after 4 weeks of therapy and 12 weeks after completion of therapy. Antiviral drug therapy should not be interrupted or discontinued if HCV RNA levels are not performed or available during treatment.

For HBsAg-positive patients who are not already on HBV suppressive therapy, the following are recommended: For patients whose HBV DNA level meets AASLD criteria for treatment, antiviral therapy for HBV should be initiated. For patients whose baseline HBV DNA level does not meet criteria for treatment, one of two approaches may be taken: Initiate prophylactic antiviral therapy for those with low or undetectable HBV DNA levels. If this course is elected, pending further data, prophylaxis should be continued until 12 weeks after completion of DAA therapy. Monitor HBV DNA levels during and immediately after DAA therapy for HCV. Antiviral treatment for HBV should be given in the event of a rise in HBV DNA >10-fold above baseline or to >1000 IU/mL in those with a previously undetectable or unquantifiable HBV DNA level

Post-Treatment Follow-Up for Patients Who Achieved a Sustained Virologic Response

Recommended Follow-Up for Patients Who Achieved a Sustained Virologic Response (SVR)	
RECOMMENDED	RATING
For patients who do not have advanced fibrosis (ie, those with Metavir stage F0, F1, or F2), recommended follow-up is the same as if they were never infected with HCV.	I, B
Assessment for HCV recurrence or reinfection is recommended only if the patient has ongoing risk for HCV infection or otherwise unexplained hepatic dysfunction develops. In such cases, a quantitative HCV-RNA test rather than an HCV-antibody test is recommended to assess for HCV recurrence or reinfection.	I, A
Surveillance for hepatocellular carcinoma with twice-yearly ultrasound examination is recommended for patients with advanced fibrosis (ie, Metavir stage F3 or F4) who achieve SVR.	I, C
A baseline endoscopy is recommended to screen for varices if cirrhosis[a] is present. Patients in whom varices are found should be treated and followed as indicated.	I, C
Assessment of other causes of liver disease is recommended for patients who develop persistently abnormal liver tests after achieving SVR.	I, C
[a] For decompensated cirrhosis, please refer to the appropriate section.	

Regimen-Specific Recommendations for Use of RAS Testing in C Practice

RECOMMENDED
Elbasvir/grazoprevir NS5A RAS testing is recommended for genotype 1a-infected, treatment-naive or -experienced patients being considered for elbasvir/grazoprevir. If present, a different regimen should be considered.
Ledipasvir/sofosbuvir NS5A RAS testing can be considered for genotype 1a-infected, treatment-experienced patients without cirrhosis being considered for ledipasvir/sofosbuvir. If clinically important[a] resistance is present, a different recommended therapy should be used. NS5A RAS testing can be considered for genotype 1a-infected, treatment-experienced patients with cirrhosis being considered for ledipasvir/sofosbuvir. If clinically important[a] resistance is present, a different recommended therapy should be used.
Sofosbuvir/velpatasvir NS5A RAS testing is recommended for genotype 3-infected, treatment-naive patients with cirrhosis and treatment-experienced patients (with or without cirrhosis) being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin should be added or sofosbuvir/velpatasvir/voxilaprevir should be used.

Daclatasvir plus sofosbuvir NS5A RAS testing is recommended for genotype 3-infected, treatment-experienced patients without cirrhosis being considered for 12 weeks of daclatasvir plus sofosbuvir. If Y93H is present, weight-based ribavirin should be added. NS5A RAS testing is recommended for genotype 3-infected, treatment-naive patients with cirrhosis being considered for 24 weeks of daclatasvir plus sofosbuvir. If Y93H is present, treatment should include weight-based ribavirin, or a different recommended therapy used.	I, B

Treatment-Naive Genotype 1a With Compensated Cirrhosis

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

Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[b] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c]	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs[b] for elbasvir	16 weeks	IIa, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Includes genotype 1a resistance-associated substitutions at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.
[c] This is a 3-tablet coformulation. Please refer to the prescribing information.

Treatment-Naive Patients Genotype 1b Without Cirrhosis		
RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL	8 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A

Treatment-Naive Genotype 1b With Compensated Cirrhosis

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

Treatment-Naive Genotype 1b Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg)[c]	12 weeks	I, A

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] This is a 3-tablet coformulation. Please refer to the prescribing information.
[c] Please see statement on FDA warning regarding the use of paritaprevir/ritonavir/ombitasvir ± dasabuvir in patients with cirrhosis.

Treatment-Naive Genotype 2 Without Cirrhosis

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

Treatment-Naive Genotype 2 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	IIa, B

[a] This is a 3-tablet coformulation. Please refer to the prescribing information.
[b] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Treatment-Naive Genotype 2 With Compensated Cirrhosis

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

Treatment-Naive Genotype 2 Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/ pibrentasvir (120 mg)[b]	12 weeks	I, B
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[c] plus sofosbuvir (400 mg)	16 to 24 weeks	IIa, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] This is a 3-tablet coformulation. Please refer to the prescribing information.
[c] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Treatment-Naive Genotype 3 Without Cirrhosis

Recommended and alternative regimens listed alphabetically for:

Treatment-Naive Genotype 3 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	I, A

[a] This is a 3-tablet coformulation. Please refer to the prescribing information.
[b] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Treatment-Naive Genotype 3 With Compensated Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for: **Treatment-Naive Genotype 3 Patients With Compensated Cirrhosis[a]**		
RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)[c]	12 weeks	I, A
ALTERNATIVE	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) when Y93H is present	12 weeks	IIa, B
Daily daclatasvir (60 mg)[d] plus sofosbuvir (400 mg) with or without weight-based ribavirin[c]	24 weeks	IIa, B

Peginterferon/Ribavirin-Experienced, Genotype 1a Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for: **Peginterferon/Ribavirin-Experienced, Genotype 1a Patients Without Cirrhosis**		
RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[a] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	DURATION	RATING

Peginterferon/Ribavirin-Experienced, Genotype 1a Patients With Compensated Cirrhosis

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

Peginterferon/Ribavirin-Experienced, Genotype 1a Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[b] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c]	12 weeks	I, B

Decompensated Cirrhosis Genotype 1, 4, 5, or 6 Infection

Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1, 4, 5, or Infection and Are Ribavirin Eligible

RECOMMENDED	DURATION	RATIN
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[c]	12 weeks	I, A
Genotype 1 or 4 infection only: Daily daclatasvir (60 mg)[e] plus sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	I,

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, includin with hepatocellular carcinoma.
[b] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.
[c] Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis; increase as toler
[d] Only available data for genotype 6 are in patients with compensated cirrhosis.
[e] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P4 inducers and inhibitors, respectively. Please refer to the prescribing information for daclatasvir.

Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1, 4, 5, or 6 Infection and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	24 weeks	I, A[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A[c]
Genotype 1 or 4 infection only: Daily daclatasvir (60 mg)[d] plus sofosbuvir (400 mg)	24 weeks	II, 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 genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.
[c] Only available data for genotype 6 are in patients with compensated cirrhosis.
[d] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information for daclatasvir.

Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] and Genotype 1, 4, 5, or 6 Infection in Whom Prior Sofosbuvir- or NS5A-Based Treatment Failed

RECOMMENDED	DURATION	RATING
Prior sofosbuvir-based treatment failure 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[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[c]	24 weeks	II, C[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] Only available data for genotype 6 are in patients with compensated cirrhosis.
[c] Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis.
[d] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.

Recommended Regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 2 or 3 Infection and Are Ribavirin Eligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin	12 weeks	I, A
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	II, B

[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] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information for daclatasvir.

Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 2 or 3 Infection and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	24 weeks	II, 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] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information for daclatasvir.

Recommendations for Patients With CKD Stage[a] 1, 2, or 3

RECOMMENDED	RATING
No dose adjustment is required when using: • Daclatasvir (60 mg)[b] • Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) • Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c] • Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) • Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) • Simeprevir (150 mg) • Fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/ voxilaprevir (100 mg) • Sofosbuvir (400 mg)	I, A

[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] Refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.
[c] This is a 3-tablet coformulation. Please refer to the prescribing information.

ecommended regimens listed by evidence level and alphabetically for:

atients With CKD Stage[a] 4 or 5 (eGFR <30 mL/min or End-Stage Renal isease)

RECOMMENDED	GENOTYPE	DURATION	RATING
ily fixed-dose combination of elbasvir (50 mg)/grazoprevir 00 mg)	1a, 1b, 4	12 weeks	I, B
ily fixed-dose combination of glecaprevir (300 g)/pibrentasvir (120 mg)[b]	1, 2, 3, 4, 5, 6	8 to 16 weeks[c]	I, B[c]

Chronic kidney disease (CKD) stages: 1 = normal (eGFR >90 mL/min); 2 = mild CKD (eGFR 60-89 mL/min); 3 = oderate CKD (eGFR 30-59 ml/min); 4 = severe CKD (eGFR 15-29 mL/min); 5 = end-stage CKD (eGFR <15 mL/min)

This is a 3-tablet coformulation. Please refer to the prescribing information.

Patients in this group should be treated as would patients without CKD. Duration of glecaprevir/pibrentasvir should be sed on presence of cirrhosis and prior treatment experience (please refer to appropriate section). As such, strength rating may be lower for certain subgroups.

Table 7. Treatment recommendations for HCV-monoinfected or HCV/HIV-coinfected patients with chronic hepatitis C without cirrhosis, including treatment-naïve patients (defined as patients who have never been treated for their HCV infection) and treatment-experienced patients (defined as patients who were previously treated with pegylated IFN-α and ribavirin; pegylated IFN-α, ribavirin and sofosbuvir; or sofosbuvir and ribavirin).

Patients	Prior treatment experience	SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
Genotype 1a	Treatment-naïve	12 wk	8 wk	No	8-12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	8 wk	No	No	12 wk (HCV RNA ≤800,000 IU/ml)	No
Genotype 1b	Treatment-naïve	12 wk	8 wk	No	8-12 wk	8 wk (F0-F2) 12 wk (F3)	8 wk (F0-F2) 12 wk (F3)
	Treatment-experienced	12 wk	8 wk	No	12 wk	12 wk	12 wk
Genotype 2	Treatment-naïve	12 wk	8 wk	No	No	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 3	Treatment-naïve	12 wk	8 wk	No	No	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 4	Treatment-naïve	12 wk	8 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 5	Treatment-naïve	12 wk	8 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 6	Treatment-naïve	12 wk	8 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No

DAA, direct-acting antiviral; DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX: voxilaprevir.

Table 8. Treatment recommendations for HCV-monoinfected or HCV/HIV-coinfected patients with chronic hepatitis C with compensated (Child-Pugh A) cirrhosis, including treatment-naïve patients (defined as patients who have never been treated for their HCV infection) and treatment-experienced patients (defined as patients who were previously treated with pegylated IFN-α and ribavirin; pegylated IFN-α, ribavirin and sofosbuvir; or sofosbuvir and ribavirin).

Patients	Prior treatment experience	SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
Genotype 1a	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	12 wk	No	No	12 wk (HCV RNA ≤800,000 IU/ml)	No
Genotype 1b	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk	12 wk
	Treatment-experienced	12 wk	12 wk	No	12 wk	12 wk	12 wk
Genotype 2	Treatment-naïve	12 wk	12 wk	No	No	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 3	Treatment-naïve	No	12 wk	12 wk	No	No	No
	Treatment-experienced	No	16 wk	12 wk	No	No	No
Genotype 4	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 5	Treatment-naïve	12 wk	12 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 6	Treatment-naïve	12 wk	12 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No

DAA, direct-acting antiviral; DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX: voxilaprevir.

Table 4E. Drug-drug interactions between HCV DAAs and cardiovascular drugs.

		SOF	SOF/ LDV	SOF/ VEL	OBV/ PTV/r + DSV	GZR/ EBR	SOF/ VEL/ VOX	GLE/ PIB
Anti-arrhythmics	Amiodarone	●	●	●	●	■	●	■
	Digoxin	◆	■	■	■	◆	■	■
	Vernakalant	◆	◆	◆	■	◆	◆	◆
	Flecainide	◆	◆	◆	■	◆	◆	◆
Beta-blockers	Atenolol	◆	◆	◆	◆	◆	◆	◆
	Bisoprolol	◆	◆	◆	■	◆	◆	◆
	Carvedilol	◆	■	■	■	◆	■	■
	Propranolol	◆	◆	◆	◆	◆	◆	◆
Calcium channel blockers	Amlodipine	◆	■	■	■	◆	◆	◆
	Diltiazem	◆	■	■	■	◆	■	■
	Nifedipine	◆	◆	◆	■	◆	◆	◆
Hypertension and heart failure agents	Aliskiren	◆	■	■	●	◆	●	●
	Losartan	◆	◆	◆	◆	◆	◆	◆
	Doxazosin	◆	◆	◆	■	◆	◆	◆
	Enalapril	◆	◆	◆	■	◆	■	■

غربالگری و بیماریابی ضرورت زمان

طبق مطالعات انجام شده در کشور ایران، افراد زیر در معرض خطر بوده و لازم است مورد غربالگری هپاتیت سی با anti-HCV Ab قرار گیرند و در صورت مثبت بودن این تست، بررسی تکمیلی توصیه می شود.

۱- افراد با سابقه تزریق خون و فرآورده های خونی قبل از سال ۱۳۷۵ (زمان شروع غربالگری خون)

۲- افراد با سابقه مجروحیت در جبهه خصوصا اگر همراه با جراحی، بستری در بیمارستان و دریافت خون باشد.

۳- افراد با سابقه حتی یک بار تزریق مواد مخدر

٤- افراد با سابقه زندان خصوصا سابقه زندانی در بندهای اعتیاد

٥- کلیه بیماران هموفیلی، تالاسمی و دیالیزی

افراد فوق در اولویت یک قرار می گیرند و کسانی که افزایش ALT غیرقابل توجیه با سابقه خالکوبی و یا با سابقه رفتارهای جنسی پرخطر در اولویت دوم می باشند.

توصیه های بررسی و تشخیص

جهت شروع درمان توصیه می شود اقدامات زیر انجام شود:

۱- انجام شمارش ویروس به روش کمی

۲- انجام تست تعیین ژنوتیپ هپاتیت سی

۳- انجام بیوپسی کبد و یا فیبروواسکن (ترجیحی)

٤- بررسی آزمایشگاهی روتین و سونوگرافی شکم

٥- در موارد شک به سیروز کبدی، آندوسکوپی فوقانی جهت بررسی واریس مری

٦- در بیماران با فیبروز کبدی بالا (F3 و بالاتر)، غربالگری HCC هم انجام شود.

- ✓ براساس نوع ژنوتیپ هپاتیت سی، سابقه قبلی درمان، وجود یا عدم وجود سیروز کبدی، بیماری های زمینه ای همراه، عفونت های همزمان HIV و یا HBV و ... تصمیم گیری درمان صورت می گیرد.

- ✓ درمان ژنوتیپ ۱ و ٤

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- در موارد غیرسیروز درمان های انتخابی سوفوسبویر/لدیپاسویر یا سوفوسبویر/داکلاتاسویر به مدت ۱۲ هفته می باشد.
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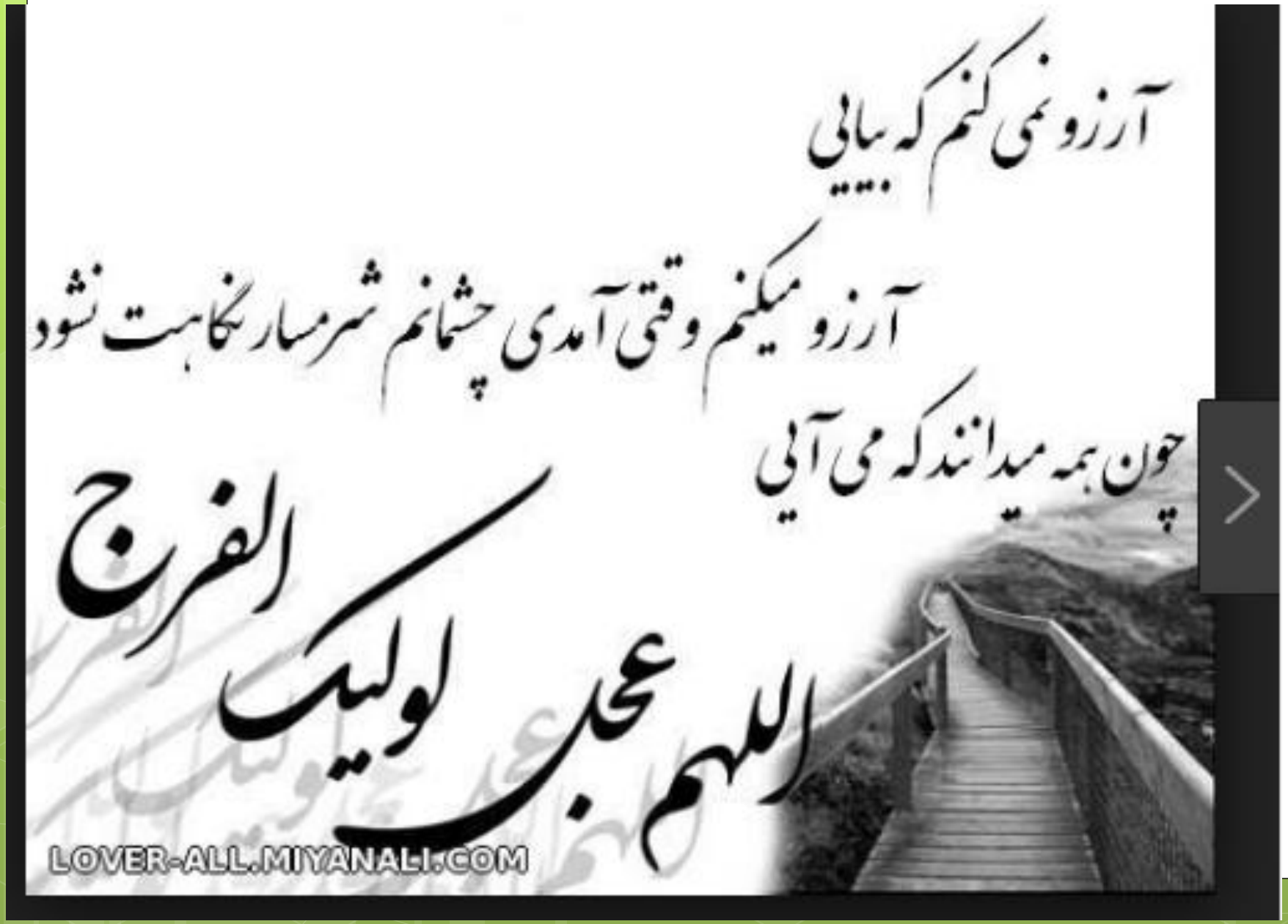
✓ درمان ژنوتیپ ۲

- در موارد غیرسیروز درمان های انتخابی سوفوسبویر/ ریباورین یا سوفوسبویرلداکلاتاسویر به مدت ۱۲ هفته می باشد.
- در موارد سیروز کبدی یا فیبروز شدید درمان های انتخابی سوفوسبویر/ ریباورین به مدت ۲٤ هفته یا سوفوسبویرلداکلاتاسویر به مدت ۱۲ هفته می باشد.
- در موارد سیروز کبدی دکمپانسه درمان انتخابی سوفوسبویرلداکلاتاسویر به مدت ۲٤ هفته همراه با ریباورین می باشد.

✓ درمان ژنوتیپ ۳

- در موارد غیرسیروز درمان انتخابی سوفوسبویرلداکلاتاسویر به مدت ۱۲ هفته می باشد.
- در موارد سیروز کبدی یا فیبروز شدید درمان انتخابی سوفوسبویرلداکلاتاسویر به مدت ۲٤ هفته همراه با ریباورین می باشد.
- در موارد سیروز کبدی دکمپانسه درمان انتخابی سوفوسبویرلداکلاتاسویر به مدت ۲٤ هفته همراه با ریباورین می باشد.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