Simplified HCV Treatment* for Treatment-Naive Adults Without Cirrhosis

Who Is *NOT* Eligible for Simplified Treatment (Without Cirrhosis)

Persons who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these individuals.)

Who Is Eligible for Simplified Treatment (Without Cirrhosis)

Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hepatitis C treatment

Pretreatment Assessment*

- Calculate FIB-4 score.
- **Cirrhosis assessment:** Liver biopsy is not required. For the purpose of this guidance, a person is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
    - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
    - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
    - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
    - Prior liver biopsy showing cirrhosis
- **Medication reconciliation:** Record current medications, including over-the-counter drugs and herbal/dietary supplements.

- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
    - Drug-drug interactions are particularly important in HIV/HCV coinfection
    - In those with HIV, the simplified treatment approach should not be used in those on tenofovir disoproxil fumarate (TDF) containing regimens with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 because of the need for additional monitoring.
- **Education:** Educate the person to be treated about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing:**
    - *Within 6 months of initiating treatment:*
        - Complete blood count (CBC)
        - Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST])
        - eGFR
    - *Any time prior to starting antiviral therapy:*
        - Quantitative HCV RNA (HCV viral load)
        - HIV antigen/antibody test
        - Hepatitis B surface antigen
    - *Before initiating antiviral therapy*:
        - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

Recommended Regimens*

- Glecaprevir (300 mg)/pibrentasvir (120 mg) to be taken with food for a duration of 8 weeks
- Sofosbuvir (400 mg)/velpatasvir (100 mg) for a duration of 12 weeks

On-Treatment Monitoring

- Inform persons taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform persons taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other individuals.
- An in-person or telehealth/phone visit may be scheduled, if needed, for support, assessment of symptoms, and/or new medications.

Post-Treatment Assessment of Cure (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for persons with elevated transaminase levels after achieving SVR.

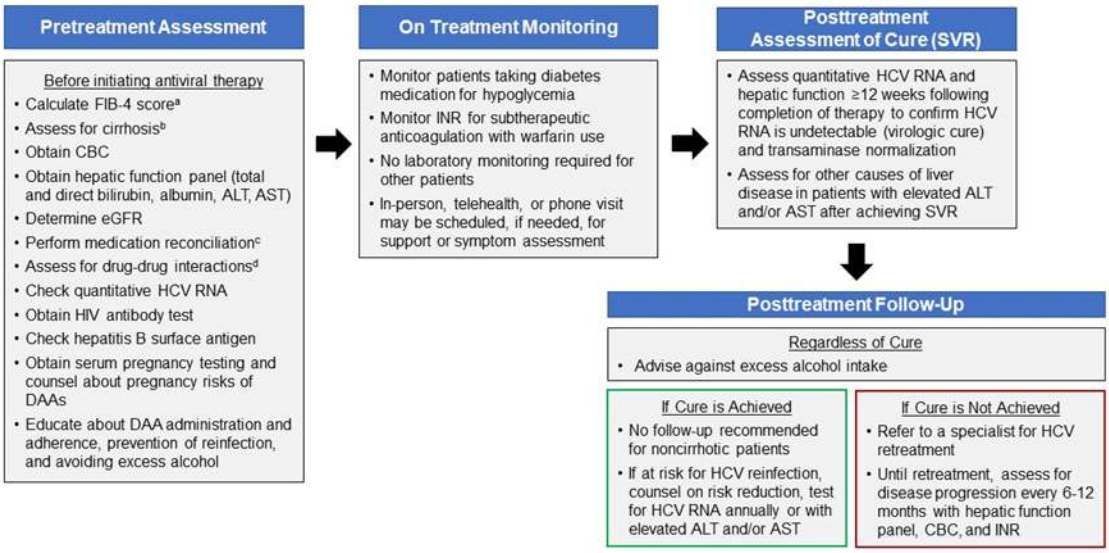
Follow-Up After Achieving Virologic Cure (SVR)

- No liver-related follow-up is recommended for persons without cirrhosis who achieve SVR.
- Persons with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Advise individuals to avoid excess alcohol use.

Follow-Up for Persons Who Do *Not* Achieve a Virologic Cure

- Persons in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Until retreatment occurs, assessment for disease progression every 6 months to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Advise individuals to avoid excess alcohol use.

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of persons with cirrhosis, can be found here.



[a] FIB-4 is a noninvasive measure of hepatic fibrosis that is calculated by: (age [years] x AST [U/L]) ÷ (platelet count [10^9/L]) x ($ALT^{1/2}$ [U/L])).

[b] A person is presumed to have cirrhosis if they have a FIB-4 score >3.25 or if they any of the following from a previously performed test: (1) transient elastography indicating cirrhosis (ie, liver stiffness >12.5 kPa); (2) noninvasive serologic test above the proprietary cutoff indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test); (3) clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3); or (4) prior liver biopsy showing cirrhosis.

[c] Medication reconciliation should record currently prescribed medications, over-the-counter drugs, and herbal/dietary supplements.

[d] Drug-drug interaction assessment should be performed using the table in the monitoring section of the HCV guidance website or the University of Liverpool drug interaction checker.

Last Update: December 19, 2023 **Last Review:** January 15, 2025

Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

Who Is *NOT* Eligible for Simplified Treatment (With Cirrhosis)

Persons who have any of the following characteristics:

- Current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/1.73 m^2) (see Persons with Renal Impairment section)
- HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these persons.)

Who Is Eligible for Simplified Treatment (With Cirrhosis)

Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment

Liver biopsy is not required. For the purpose of this guidance, a person is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.

- Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
- Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
- Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
- Prior liver biopsy showing cirrhosis

Pretreatment Assessment*

- Calculate FIB-4 score.
- **Calculate CTP score:** Persons with a CTP score ≥7 (ie, CTP class B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation:** Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
    - Drug-drug interactions are particularly important in HIV/HCV coinfection.
    - In those with HIV, the simplified treatment approach should not be used in those on tenofovir disoproxil fumarate (TDF) containing regimens with estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 because of the need of additional monitoring.
- **Education:** Educate the person to be treated about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing:**
    - *Within 3 months of initiating treatment:*
        - Complete blood count (CBC)
        - International normalized ratio (INR)
        - Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST])
        - eGFR
    - *Any time prior to starting antiviral therapy:*
        - Quantitative HCV RNA (HCV viral load)
        - HIV antigen/antibody test
        - Hepatitis B surface antigen
        - HCV genotype (if treating with sofosbuvir/velpatasvir)
    - *Before initiating antiviral therapy*:
        - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

Recommended Regimens*

- **Genotype 1-6**:
  Glecaprevir (300 mg) / pibrentasvir (120 mg) to be taken with food for a duration of 8 weeks
- **Genotype 1, 2, 4, 5, or 6**
  Sofosbuvir (400 mg) / velpatasvir (100 mg) for a duration of 12 weeks
  NOTE: Persons with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without the Y93H RAS can be treated with 12 weeks of sofosbuvir/velpatasvir. If the Y93H RAS is present, see HCV guidance for treatment recommendations.

On-Treatment Monitoring

- Clinicians may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among persons with cirrhosis receiving HCV antiviral treatment.
- Persons should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform persons taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform persons taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for support, assessment of symptoms, and/or new medications.

Post-Treatment Assessment of Cure (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for persons with elevated transaminase levels after achieving SVR.

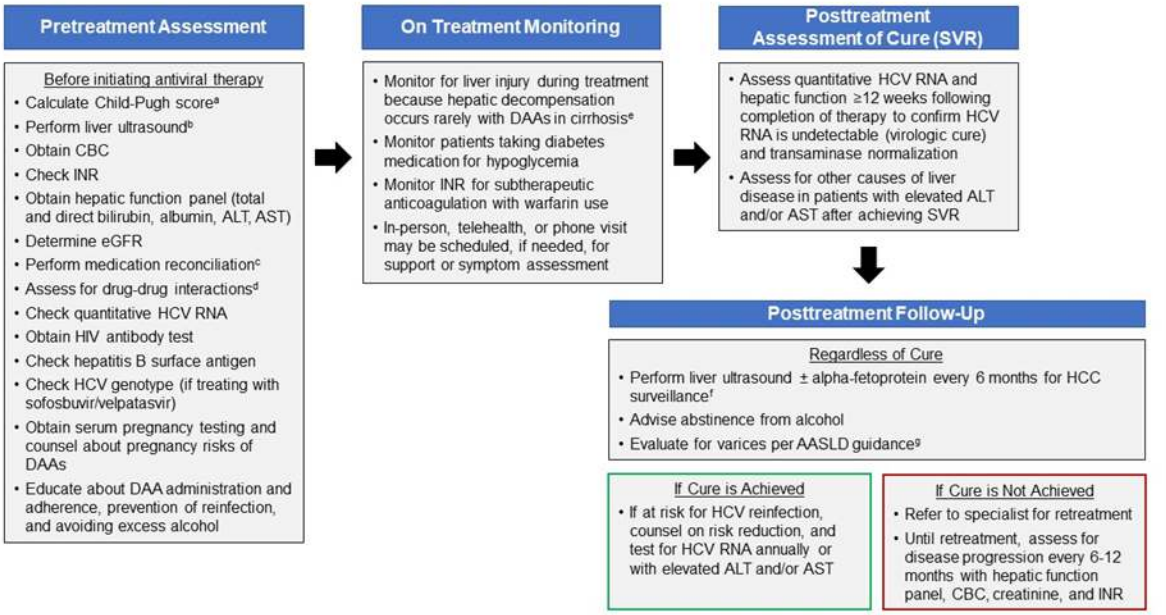
Follow-Up After Achieving Virologic Cure (SVR)

- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for persons with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis.
- Persons with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Individuals should abstain from alcohol to avoid progression of liver disease.

Follow-Up for Persons Who Do *Not* Achieve a Virologic Cure

- Persons in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for persons with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 months to 12 months with a hepatic function panel, CBC, creatinine, and INR is recommended.
- Individuals should abstain from alcohol to avoid progression of liver disease.

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment can be found here.



[a] Child-Pugh score based on presence of ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7. Persons with a Child-Pugh score ≥7 (ie, Child-Pugh B or C) have decompensated cirrhosis. This simplified treatment approach is not recommended for persons with decompensated cirrhosis.

[b] Obtain liver ultrasound within 6 months prior to initiating antiviral treatment to exclude hepatocellular carcinoma and subclinical ascites. This simplified treatment approach is not recommended for persons with hepatocellular carcinoma and/or decompensated cirrhosis.

[c] Medication reconciliation should record currently prescribed medications, over-the-counter drugs, and herbal/dietary supplements.

[d] Drug-drug interaction assessment should be performed using the table in the monitoring section of the HCV guidance website or the University of Liverpool drug interaction checker.

[e] Development of jaundice, ascites, spontaneous bacterial peritonitis, variceal hemorrhage, or hepatic encephalopathy may suggest hepatic decompensation. Persons should be referred to a specialist if they develop worsening liver blood tests (eg, total bilirubin, AST, ALT, INR), jaundice, ascites, encephalopathy, or new liver-related symptoms.

[f] Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for persons with cirrhosis, in accordance with AASLD guidance.

[g] See AASLD guidance for recommendations regarding the evaluation and management of varices.

Last update: December 19, 2023 **Last Review:** January 15, 2025