Chronic HCV Infection:
On-treatment Monitoring Guide

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Treatment of Chronic HCV

Treatment for HCV infection has evolved substantially in recent years, with the approval of new drugs with different mechanisms of action. Direct-acting antivirals (DAAs) for HCV are molecules that target specific steps within the HCV viral life cycle, thereby disrupting viral replication and resulting in viral clearance and cure.

There are four classes of HCV DAAs, which are defined by their mechanism of action and therapeutic target:

<table>
<thead>
<tr>
<th>DAA Class</th>
<th>Brief Mechanism of Action</th>
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<tbody>
<tr>
<td><strong>1</strong> NS3/4A protease inhibitors</td>
<td>Block a viral enzyme (protease) preventing processing of viral polypeptides</td>
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<tr>
<td><strong>2</strong> NS5B nucleos(t)ide polymerase inhibitors</td>
<td>Attaches to replicating viral DNA, preventing new copies from being made</td>
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<td><strong>3</strong> NS5A inhibitors</td>
<td>Blocks a virus protein, NS5A, that the virus needs during replication for viral assembly and other functions</td>
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<tr>
<td><strong>4</strong> NS5B non-nucleoside polymerase inhibitors</td>
<td>Stops HCV from replicating RNA by attaching to NS5B, which is necessary for creating new RNA</td>
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Current HCV treatments are most commonly a combination of two or more of these classes.

Treatment considerations

**Discontinue treatment if any of the following occur:**
- A 10-fold increase in ALT activity at any time during treatment
- An increase in ALT <10-fold that is accompanied by any weakness, nausea, vomiting, jaundice, or significantly increased bilirubin, alkaline phosphatase, or INR

Asymptomatic increases in ALT <10-fold should be closely monitored with repeat testing at 2-week intervals. If levels remain persistently elevated, consideration should be given to discontinuation of therapy.

Antiviral drug therapy should not be interrupted or discontinued if HCV RNA levels are not performed or available during treatment.

**HCV/HBV co-infected patients: Consider referral to specialist**
- Monitor HCV/HBV coinfected patients for HBV reactivation and hepatitis flare during HCV treatment

For HBsAg-positive patients who are not already on HBV suppressive therapy, the following are recommended:
- Antiviral therapy for HBV should be initiated
- Initiate prophylactic antiviral therapy for those with low or undetectable HBV DNA levels. If this course is selected, 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
Recommendations for On-treatment Monitoring

Once all of the necessary pre-treatment workup has been completed for a patient diagnosed with HCV infection, the following on-treatment monitoring steps are recommended for patients receiving DAAs:

### Treatment Initiation

- **General Monitoring**:
  - Clinic visits or telephone contact as clinically indicated during treatment to:
    - Ensure medication adherence
    - Monitor for AEs
    - Monitor for potential DDIs with newly prescribed medications

### Patient-specific Monitoring

- **Treatment Initiation**:
  - Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia
    - Monitoring for hypoglycemia is recommended
  - Inform patients taking warfarin of the potential for changes in their anticoagulation status
    - INR monitoring for subtherapeutic anticoagulation is recommended
  - For patients with compensated cirrhosis:
    - Consider ordering blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment
    - Patients 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

### General Monitoring

- **End of Treatment**:
  - Consider a quantitative HCV viral load test

### Treatment-specific Monitoring

- **Treatment Week 8**:
  - More frequent assessment for drug-related AEs (eg, CBC for patients receiving ribavirin) as clinically indicated

- **Treatment Week 12**:

- **Treatment Week 16**:

See full prescribing information for treatment-specific monitoring recommendations.
References


Abbreviations

**AASLD**
American Association for the Study of Liver Diseases

**AE**
Adverse event

**ALT**
Alanine aminotransferase

**AST**
Aspartate aminotransferase

**CBC**
Complete blood count

**DAA**
Direct-acting antivirals

**DDI**
Drug-drug interaction

**DNA**
Deoxyribonucleic acid

**HBSAG**
Hepatitis B surface antigen

**HCV**
Hepatitis C virus

**IDSA**
Infectious Diseases Society of America

**INR**
International normalized ratio

**NS3/4A**
Non-structural protein 3/4A

**NS5A**
Non-structural protein 5A

**NS5B**
Non-structural protein 5B

**RNA**
Ribonucleic acid

**HBV**
Hepatitis B virus