**Screening and testing**

**Whom to test**
- Patients wanting to be tested
- Patients having 1 or more of the following risk factors:
  - Vietnam-era veteran
  - Transfusion before 1992
  - Intravenous drug use
  - Exposure of skin to blood
  - Multiple sex partners
  - Hemodialysis
  - Tattoos/Piercings
  - Nasal cocaine use
  - Unexplained liver disease
  - Unexplained abnormal ALT
  - Heavy alcohol use

**Initial testing**
- Anti-HCV by ELISA
- AST/ALT (if not done previously)

**Pretest counseling**
- For risk behaviors
- Limitations of ELISA test
- Schedule test and follow-up visit

**Posttest strategy**

<table>
<thead>
<tr>
<th>Result of Anti-HCV by ELISA</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative</strong></td>
<td>- Patient is unlikely to be infected with HCV unless immunocompromised</td>
</tr>
<tr>
<td></td>
<td>- If suspicion is high (patient has risk factors and is immunocompromised or patient has risk factors and acute hepatitis), obtain HCV RNA by PCR</td>
</tr>
<tr>
<td><strong>Indeterminate</strong></td>
<td>- Uncertain whether patient is infected with HCV (could be in process of forming antibodies, or other factors unrelated to HCV are present)</td>
</tr>
<tr>
<td></td>
<td>- Obtain HCV RNA by PCR</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td>- Patient may be infected with HCV; test does not indicate whether infection is acute, chronic, or resolved; result may be false positive</td>
</tr>
<tr>
<td></td>
<td>- Obtain HCV RNA by PCR; positive result confirms that patient has active HCV</td>
</tr>
</tbody>
</table>

**Candidates for antiviral treatment**
- All patients with positive HCV RNA are potential candidates
- Treatment should be offered to patients with liver histology showing more than portal fibrosis (including those with compensated cirrhosis) and to those without contraindications

**Antiviral treatment eligibility**

<table>
<thead>
<tr>
<th>Contraindications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interferon</strong> (if contraindicated, patient should not receive any therapy as ribavirin alone is not useful)</td>
<td>- Platelet count &lt;70,000 cells/µL</td>
</tr>
<tr>
<td></td>
<td>- ANC &lt;1,500 cells/µL</td>
</tr>
<tr>
<td></td>
<td>- Life-determining extrahepatic disease (malignancy, unstable angina, severe COPD)</td>
</tr>
<tr>
<td></td>
<td>- Clinically decompensated liver disease</td>
</tr>
<tr>
<td></td>
<td>- Uncontrolled autoimmune disorders</td>
</tr>
<tr>
<td></td>
<td>- Pregnancy or planned pregnancy in patient or partner, or unwillingness to use birth control</td>
</tr>
<tr>
<td></td>
<td>- Documented nonadherence to prior therapy, or failure to complete pretreatment evaluation appointments or procedures</td>
</tr>
<tr>
<td></td>
<td>- Inability to self-administer or to arrange administration of parenteral medication</td>
</tr>
<tr>
<td></td>
<td>- Severe uncontrolled psychiatric disease, particularly depression with current suicidal risk</td>
</tr>
<tr>
<td></td>
<td>- Ongoing injection drug use</td>
</tr>
<tr>
<td></td>
<td>- Ongoing alcohol abuse</td>
</tr>
<tr>
<td>Pretreatment assessment</td>
<td>Necessary evaluations</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------</td>
</tr>
</tbody>
</table>
| **Ribavirin** (if contraindicated, interferon monotherapy can be considered) | ● Medical history  
 ● Psychiatric history  
 ● Screening for depression and alcohol use  
 ● Biochemical markers of liver injury and synthetic dysfunction  
   ○ Serum ALT  
   ○ Serum albumin  
   ○ Serum bilirubin (particularly direct)  
   ○ Prothrombin time  
 ● Hemoglobin, hematocrit, total WBC, WBC with differential and platelet count  
 ● Thyroid function tests  
 ● Serum creatinine  
 ● Serum glucose or HbA1C in diabetic patients  
 ● Pregnancy test (in women of childbearing potential)  
 ● HIV serology  
 ● Serum HBsAg, anti-HBs, anti-HBc (total), and anti-HAV (total)  
 ● Quantitative HCV RNA  
 ● HCV genotype  
 ● Previous antiviral therapies and response  
 ● ECG in preexisting cardiac disease |

| Highly recommended evaluations | ● Liver biopsy to stage severity of disease (especially in patients with genotype 1 infection)  
 ● Eye examination for retinopathy in patients with diabetes or hypertension  
 ● Serum ferritin, iron saturation, and serum ANA  
 ● Urine toxicity screen for opiates, cocaine, and amphetamine |

| Pretreatment counseling | ● Cessation of alcohol use  
 ● Likelihood of achieving SVR  
 ● Side effects of therapy |
|-------------------------|----------------------|
| **Interferon** | ● Flulike symptoms  
 ● Bone marrow suppression (greater with peginterferon)  
 ● Aggravation of autoimmune disorders  
 ● Neuropsychiatric symptoms  
 ● Seizures  
 ● Acute cardiac and renal failure  
 ● Retinopathy  
 ● Interstitial pulmonary fibrosis |

| **Ribavirin** | ● Hemolytic anemia  
 ● Significant teratogen  
 ● Rash(es)  
 ● Headaches  
 ● Shortness of breath  
 ● GI effects |
**Antiviral treatment strategy**

<table>
<thead>
<tr>
<th>Genotype 1</th>
<th>Genotype 2-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Contraception • Adequate contraception needed during treatment and for 6 months after completion of treatment • Importance of adherence</td>
<td></td>
</tr>
</tbody>
</table>

**Peginterferon alfa 2a (Pegasys)** 180 mcg SC once weekly (regardless of weight) OR

**Peginterferon alfa 2b (Peg-Intron)** 1.5 mcg/kg SC once weekly up to 150 mcg/week AND

See **Peginterferon chart** (below)

**Ribavirin (Rebetol, Copegus)**

See **Ribavirin chart** (below)

**Duration of therapy** • If 4-week HCV RNA undetectable (RVR), 24 weeks may be sufficient • If no RVR, but 12-week HCV RNA undetectable or decreased by $>2 \log_{10}$ (EVR), 48 weeks is sufficient • If no RVR or EVR, extending duration to 72 weeks may be beneficial if HCV RNA undetectable at week 24 (if patient has advanced fibrosis and depending on tolerance of therapy)

**Genotype 2-3** • Peginterferon alfa 2a (Pegasys) 180 mcg SC once weekly (regardless of weight) OR

• Peginterferon alfa 2b (Peg-Intron) 1.5 mcg/kg SC once weekly up to 150 mcg/week AND

• Ribavirin 800 mg QD (400 mg PO BID)

See **Ribavirin chart** (below)

**Duration of therapy** • Standard treatment duration is 24 weeks • For patients with low pretreatment HCV RNA (<600,000 IU/mL) who are not tolerating therapy, 16 weeks of treatment may be sufficient • For patients with genotype 3 and high viral load (>600,000 IU/mL) or steatosis, treatment beyond 24 weeks may improve response

**Follow-up laboratory monitoring** • Hemoglobin, hematocrit, WBC with differential and platelet count, creatinine • Serum ALT • Pregnancy test • TSH • Blood glucose • HCV RNA by quantitative or qualitative assay

• At week 1 or 2, at week 4, then every 1-2 months • At month 1, then every 1-2 months • Monthly during therapy and for 6 months after completing therapy • At least every 12 weeks during therapy • At least every 12 weeks during therapy • At week 4, 12, and 24 during therapy, at end of therapy, and 6 months after completion of therapy
<table>
<thead>
<tr>
<th>Hemoglobin Level</th>
<th>Therapy Adjustments</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;8.5 g/dL</td>
<td>Peginterferon: Do not modify dosage; Ribavirin: Discontinue until resolution</td>
</tr>
<tr>
<td>8.5-10 g/dL</td>
<td>Peginterferon: Do not modify dosage; Ribavirin: Decrease by 200 mg/day and/or consider erythropoietin, particularly for patients who are cirrhotic, posttransplant, or HIV/HCV coinfected</td>
</tr>
<tr>
<td>10-11 g/dL</td>
<td>Peginterferon: Do not modify dosage; Ribavirin: If no or minimal symptoms, do not modify dosage; If symptomatic, decrease by 200 mg/day and/or consider erythropoietin, particularly for patients who are cirrhotic, posttransplant, or HIV/HCV coinfected</td>
</tr>
</tbody>
</table>

Candidates for erythropoietin:
- Rule out other causes of anemia
- Anemia persists at 2 weeks after reducing ribavirin
- No hypertension

Dosage:
- Epoetin alfa 40,000 units SC weekly
- Darbepoetin alfa 200 mcg SC every other week

Goal:
- Hemoglobin 12 g/dL

Adjustments according to CBC changes:
- Hemoglobin 8.5-10 g/dL
- Hemoglobin 10-11 g/dL
- Hemoglobin <8.5 g/dL
### Endpoints of HCV therapy

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RVR:</strong></td>
<td>HCV RNA &lt;50 IU/mL at week 4 into treatment</td>
</tr>
<tr>
<td><strong>EVR:</strong></td>
<td>&gt;2 log_{10} reduction from baseline HCV RNA at week 12 of treatment</td>
</tr>
<tr>
<td><strong>ETR:</strong></td>
<td>Undetectable HCV RNA at completion of treatment</td>
</tr>
<tr>
<td><strong>SVR:</strong></td>
<td>Undetectable HCV RNA at week 24 after completion of treatment</td>
</tr>
<tr>
<td><strong>Relapse:</strong></td>
<td>Undetectable viremia during or at the end of treatment, but HCV RNA is detectable after treatment is stopped</td>
</tr>
<tr>
<td><strong>Nonresponse:</strong></td>
<td>Detectable HCV RNA throughout treatment</td>
</tr>
</tbody>
</table>

| WBC <1,500 | Peginterferon alfa 2b  
Reduce dosage by 50% and reevaluate  
Ribavirin  
Do not modify dosage |
| <1000 | Peginterferon alfa 2b  
Discontinue until resolution  
Ribavirin  
Do not modify dosage |
| ANC <750 | Peginterferon  
Reduce peginterferon alfa 2a dosage to 135 mcg/week and reevaluate  
Reduce peginterferon alfa 2b dosage by 50% and reevaluate  
Ribavirin  
Do not modify dosage |
| <500 | Peginterferon  
Discontinue until resolution  
Ribavirin  
Do not modify dosage  
Consider G-CSF for patients who are cirrhotic, posttransplant, or HIV/HCV coinfectected, particularly if neutropenia persists despite peginterferon dosage reduction |
| Platelets <80,000 | Peginterferon  
Reduce peginterferon alfa 2b dosage by 50% and reevaluate  
Ribavirin  
Do not modify dosage |
| <50,000 | Peginterferon  
Reduce peginterferon alfa 2a dosage to 90 mcg/week and reevaluate  
Discontinue peginterferon alfa 2b until resolution  
Ribavirin  
Do not modify dosage |
| <25,000 | Peginterferon  
Discontinue until resolution  
Ribavirin  
Do not modify dosage |
Peginterferon Dosing (HCV Genotype 1, 2, 3)

<table>
<thead>
<tr>
<th>Weight (lbs)</th>
<th>Vial Size (mcg/0.5 mL)</th>
<th>Dose (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;88</td>
<td>50</td>
<td>0.5</td>
</tr>
<tr>
<td>88-110</td>
<td>80</td>
<td>0.4</td>
</tr>
<tr>
<td>111-141</td>
<td>80</td>
<td>0.5</td>
</tr>
<tr>
<td>142-166</td>
<td>120</td>
<td>0.4</td>
</tr>
<tr>
<td>167-187</td>
<td>120</td>
<td>0.5</td>
</tr>
<tr>
<td>&gt;187</td>
<td>150</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Ribavirin Dosing (HCV Genotype 1)

<table>
<thead>
<tr>
<th>Weight (lbs)</th>
<th>Total Daily Dosage</th>
<th>Dosing Schedule</th>
</tr>
</thead>
</table>
| ≤165         | 1,000 mg QD        | 2 (200 mg) tablets PO morning
               |                    | 3 (200 mg) tablets PO evening |
| >165         | 1,200 mg QD        | 3 (200 mg) tablets PO BID |

List of Abbreviations for Quicknotes

AFP = alpha-fetoprotein
ALT = alanine aminotransferase
ANA = antinuclear antibody
ANC = absolute neutrophil count
AST = aspartate aminotransferase
BID = twice daily
bpm = beats per minute
BUN = blood urea nitrogen
CABG = coronary artery bypass graft
CBC = complete blood count
COPD = chronic obstructive pulmonary disease
CTP = Child-Turcotte-Pugh
CT = computed tomography
ECG = electrocardiogram
EGD = esophagogastroduodenoscopy (upper endoscopy)
ELISA = enzyme-linked immunosorbent assay
ER = emergency room
ETR = end-of-treatment response
EVR = early virologic response
G-CSF = granulocyte colony-stimulating factor
GI = gastrointestinal
Anti-HAV = antibody to the hepatitis A virus
HbA1c = glycosylated hemoglobin (test)
Anti-HBc = antibody to the hepatitis B core antigen
Anti-HBs = antibody to the hepatitis B surface antigen
HBsAg = hepatitis B surface antigen
HCC = hepatocellular carcinoma
HCV = hepatitis C virus
HCV-RNA=hepatitis C virus ribonucleic acid (viral particle)
HVPG = hepatic venous pressure gradient
IV = intravenous
LVP = large-volume paracentesis
MAP = mean arterial pressure
MELD = Model for End-Stage Liver Disease (score)
MI = myocardial infarction
MRI = magnetic resonance imaging
NSAIDs = nonsteroidal antiinflammatory drugs
PCR = polymerase chain reaction
PMN = polymorphonuclear (cells)
PO = orally
QD = once daily
RBC = red blood cell (count)
RFA = radiofrequency ablation
RVR = rapid virologic response
SC = subcutaneous
SVR = sustained virologic response
THS = thyroid-stimulating hormone
TID = 3 times daily
TIPS = transjugular intrahepatic portosystemic shunt
TMP-SMX = trimethoprim-sulfamethoxazole
WBC = white blood cell (count)

Source: VA Hepatitis C Resources Centers