**TABLE 362-7 INDICATIONS AND RECOMMENDATIONS FOR ANTIVIRAL THERAPY OF CHRONIC HEPATITIS C[a]**

**Standard Indications for Therapy**

Detectable HCV RNA (with or without elevated ALT)

Portal/bridging fibrosis or moderate to severe hepatitis on liver biopsy (the necessity of a pretreatment biopsy is no longer embraced universally)

Indications for IFN/ribavirin-based therapy apply to adults as well as to children age 2–17, in whom treatment may be considered at reduced weight-based doses (see product inserts); protease inhibitors are not recommended for children age <18 years

**Retreatment Recommended**

**Genotype 1**

Relapsers, partial responders, or nonresponders after a previous course of standard IFN monotherapy or combination standard IFN/ribavirin therapy or PEG IFN/ribavirin

A course of PEG IFN/ribavirin plus protease inhibitor as below

**Genotypes 2, 3, 4**

Relapsers after a previous course of standard IFN monotherapy or combination standard IFN/ribavirin therapy

A course of PEG IFN plus ribavirin

Nonresponders to a previous course of standard IFN monotherapy or combination standard IFN/ribavirin therapy

A course of PEG IFN plus ribavirin—more likely to achieve a sustained virologic response in white patients without previous ribavirin therapy, with low baseline HCV RNA levels, with a ≥2-$\log_{10}$ reduction in HCV RNA during previous therapy, with genotypes 2 and 3, and without reduction in ribavirin dose

**Antiviral Therapy Management Decisions Made on an Individual Basis**

Children (age <18 years)—protease inhibitors not recommended.

Age >70 (in protease inhibitor trials, telaprevir trials included patients age 18–70; boceprevir trials included patients >18 years of age [no upper age cutoff])

Mild hepatitis on liver biopsy

Persons with severe renal insufficiency (require reduced doses of PEG IFN and ribavirin)

**Long-Term Maintenance Therapy Recommended**

Cutaneous vasculitis and glomerulonephritis associated with chronic hepatitis C

**Long-Term Maintenance Therapy in Nonresponders Not Recommended**

**Antiviral Therapy Not Recommended**

Decompensated cirrhosis (except, perhaps, in transplantation centers with experience in graded escalation, low-dose treatment to achieve undetectable HCV RNA prior to transplantation; results are mixed)

Pregnancy (teratogenicity of ribavirin)

Contraindications to use of antiviral medications

**Therapeutic Regimens**

**HCV genotype 1**

**TREATMENT-NAÏVE (telaprevir and boceprevir) and PRIOR RELAPSERS (telaprevir)**

PEG IFN-α2a 180 μg weekly plus weight-based ribavirin 1000 mg/d (<75 kg) to 1200 mg/d (≥75 kg) or

PEG IFN-α2b 1.5 μg/kg weekly plus weight-based ribavirin 800 mg/d (≤65 kg), 1000 mg/d (>65–85 kg), 1200 mg/d (>85–105 kg), or 1400 mg/d (>105 kg)

Plus response-guided therapy with a protease inhibitor consisting of either:

Boceprevir 800 mg three times daily with food started after a lead-in treatment of 4 weeks with PEG IFN–ribavirin

- Patients with undetectable HCV RNA at 8 and 24 weeks should receive triple-drug therapy (PEG IFN, ribavirin, boceprevir) through week 28 (4 weeks of PEG IFN–ribavirin then 24 weeks of triple-drug therapy). If HCV RNA is detectable at 4 weeks, continuing therapy through 48 weeks (4 weeks of PEG IFN–ribavirin then 44 weeks of triple-drug therapy) may increase the sustained response rate.
- Patients with detectable HCV RNA at 8 weeks and undetectable at 24 weeks should receive triple-drug therapy (PEG IFN, ribavirin, boceprevir) through week 36 (4 weeks of PEG IFN–ribavirin then 32 weeks of triple-drug therapy) followed by a return to PEG IFN–ribavirin for 12 more weeks, for a total treatment duration of 48 weeks.
- Patients with cirrhosis who are treatment-naive and have undetectable HCV RNA at weeks 8 and 24 should continue triple-drug therapy (PEG IFN, ribavirin, boceprevir) through 48 weeks (4 weeks of PEG IFN–ribavirin then 44 weeks of triple-drug therapy).
- Stopping rules for futility: HCV RNA ≥100 IU/mL at week 12 or any detectable HCV RNA at week 24

*or*

Telaprevir 750 mg three times daily with fatty food started at the beginning of therapy without a PEG IFN–ribavirin lead-in

- Patients with undetectable HCV RNA at 4 and 12 weeks should receive triple-drug therapy (PEG IFN, ribavirin, telaprevir) for 12 weeks then PEG IFN and ribavirin for another 12 weeks, for a total of 24 weeks.
- Patients with detectable HCV RNA at 4 or 12 weeks and undetectable at 24 weeks should receive triple-drug therapy (PEG IFN, ribavirin, telaprevir) for 12 weeks, then PEG IFN–ribavirin for another 36 weeks, for a total treatment duration of 48 weeks.
- Patients with cirrhosis who are treatment-naïve and have undetectable HCV RNA at 4 and 12 weeks should receive triple-drug therapy for 12 weeks then PEG IFN–ribavirin for another 36 weeks, for a total treatment duration of 48 weeks.
- Stopping rules for futility: HCV RNA >1000 IU/mL at week 4 or 12 or any detectable HCV RNA at week 24

**TREATMENT-EXPERIENCED**

PEG IFN-α2a 180 μg weekly plus weight-based ribavirin 1000 mg/d (<75 kg) to 1200 mg/d (≥75 kg) or

PEG IFN-α2b 1.5 μg/kg weekly plus weight-based ribavirin 800 mg/d (≤65kg), 1000 mg/d (>65–85 kg), 1200 mg/d (>85–105 kg), or 1400 mg/d (>105 kg)

Plus a protease inhibitor consisting of either:

Response-guided therapy with boceprevir 800 mg three times daily with food started after a lead-in treatment of 4 weeks with PEG IFN–ribavirin

- For prior relapsers and partial responders (HCV RNA reduction of ≥2 $\log_{10}$ during previous therapy), follow the response-guided algorithm below; for prior null responders (HCV RNA reduction <2 $\log_{10}$ during previous therapy), a full 48-week course of therapy (4-week PEG IFN–ribavirin lead-in, followed by 44 weeks of triple-drug therapy [PEG IFN, ribavirin, boceprevir]) is recommended.

(*Continued*)