TABLE 215e-1 ANTIVIRAL CHEMOTHERAPY AND CHEMOPROPHYLAXIS (*CONTINUED*)

Infection	Drug	Route	Dosage	Comment
	Sofosbuvir[g]	Oral	HCV genotypes 1, 4, 5, and 6: 400 mg qd with daily weight-based ribavirin (1000 mg [<75 kg] to 1200 mg [>75 kg]) and weekly pegylated IFN for 12 weeks. Genotypes 2 and 3: 400 mg qd with daily weight-based ribavirin for 12 and 24 weeks, respectively	Sofosbuvir is generally well tolerated, and most common side effects have been attributable to concomitantly administered IFN and ribavirin. Sofosbuvir is recommended in triple combination with pegylated IFN and ribavirin as first-line therapy for genotypes 1, 4, 5, and 6, with SVRs in 89–97% of treatment-naïve patients, and in double combination with ribavirin for genotypes 2 and 3.
	Simeprevir[g]	Oral	Alternative regimen for genotypes 1 and 4: 150 mg qd for 12 weeks plus daily ribavirin and weekly pegylated IFN for 24 weeks and for 24–48 weeks, respectively	Simeprevir has supplanted the first-generation protease inhibitors boceprevir and telaprevir. Its metabolism by cytochrome CYP3A can result in interactions with other drugs. Photosensitivity and reversible hyperbilirubinemia are associated toxicities. Testing for the Q80K-resistant variant should be carried out since this variant is present in one-third of HCV genotype 1a infections. Triple combinations with pegylated IFN and ribavirin result in SVRs in 80% of genotype 1 infections without Q80K.
Chronic hepatitis D	IFN-α2a or IFN-α2b Pegylated IFN-α2b Pegylated IFN-α2a	SC SC SC	9 million units thrice weekly × 12 months 1.5 μg weekly × 48 weeks 180 μg weekly × 48 weeks	The overall efficacy and the optimal regimen and duration of therapy are not fully established. Sustained SVRs have been seen in 25–30% of patients for IFN-α and in 17–43% for pegylated IFN-α.

[a]For detailed weight recommendations and for children <1 year of age, see *www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm*. [b]Amantadine and rimantadine are not recommended for routine use because of widespread resistance in currently circulating A/H3N2 and pandemic A/H1N1 viruses. Their use may be considered if sensitivities become reestablished. [c]Not approved for this indication by the U.S. Food and Drug Administration (FDA). [d]Approved by the FDA for treatment of HIV-infected individuals. [e]Acyclovir suspension (15 mg/kg PO, to a maximum of 200 mg per dose) given for 7 d has been reported to be effective in treatment of primary herpetic gingivostomatitis in children. [f]Active ingredient: benzyl alcohol. Available without prescription. [g]Consult *www.hcvguidelines.org* for recommendations regarding treatment of null or partial responders to IFN regimens or of patients ineligible to receive IFN.

Abbreviations: ALT, alanine aminotransferase; CMV, cytomegalovirus; CPK, creatine phosphokinase; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HSV, herpes simplex virus; IFN, interferon; RGT, response-guided therapy; RSV, respiratory syncytial virus; SVR, sustained virologic response; VZV, varicella-zoster virus.

Zanamivir and oseltamivir have been approved by the U.S. Food and Drug Administration (FDA) for treatment of influenza in adults and in children (those ≥7 years old for zanamivir and those ≥1 year old for oseltamivir) who have been symptomatic for ≤2 days. Oseltamivir is approved for prophylaxis of influenza in individuals ≥1 year of age and zanamivir for those ≥5 years of age (Table 215e-1). Guidelines for the use of oseltamivir in children <1 year of age can be accessed through the CDC website, as noted in the footnote to Table 215e-1.

Peramivir is an investigational neuraminidase inhibitor that can be administered intravenously to patients for whom such an intervention is considered necessary. It has been approved in Japan, China, and South Korea but not in the United States, where it has been available in clinical trials through BioCryst Pharmaceuticals. Oseltamivir-resistant viruses generally exhibit reduced sensitivity to peramivir.

Laninamivir octonoate is an investigational neuraminidase that has been approved in Japan. It is the prodrug of laninamivir, which is administered by oral inhalation and has a prolonged half-life of ~3 days. In limited studies, it has been investigated as single-dose therapy for influenza; its effects were similar to those obtained with multiple dosing of zanamivir or oseltamivir.

AMANTADINE AND RIMANTADINE

Amantadine and the closely related compound rimantadine are primary symmetric amines that have antiviral activity limited to influenza A viruses. Amantadine and rimantadine have a long history of efficacy in the prophylaxis and treatment of influenza A infections in humans. However, high frequencies of resistance to these drugs were noted among influenza A/H3N2 viruses in the 2005–2006 influenza season and continued to be seen in 2013–2014. The pandemic A/H1N1 viruses that circulated in 2009–2010 were also resistant to amantadine and rimantadine, and circulating influenza A/H1N1 viruses in the 2013–2014 season were largely resistant. Therefore, these agents are no longer recommended unless the sensitivity of the particular isolate of influenza A virus is known, in which case their use may be considered. Amantadine and rimantadine act through inhibition of the ion channel function of the influenza A M2 matrix protein, on which uncoating of the virus depends. A substitution of a single amino acid at critical sites in the M2 protein can result in a virus that is resistant to amantadine and rimantadine.

Amantadine and rimantadine have been shown to be effective in the prophylaxis of influenza A in large-scale studies of young adults and in less extensive studies of children and elderly persons. In such studies, efficacy rates of 55–80% in the prevention of influenza-like illness were noted, and even higher rates were reported when virus-specific attack rates were calculated. Amantadine and rimantadine have also been found to be effective in the treatment of influenza A infection in studies involving predominantly young adults and, to a lesser extent, children. Administration of these compounds within 24–72 h after the onset of illness has resulted in a reduction of the duration of signs and symptoms by ~50% compared with that in placebo recipients. The effect on signs and symptoms of illness is superior to that of commonly used antipyretic-analgesic agents. Only anecdotal reports are available concerning the efficacy of amantadine or rimantadine in the prevention or treatment of complications of influenza (e.g., pneumonia).

Amantadine and rimantadine are available only in oral formulations and are ordinarily administered to adults once or twice daily, with a dosage of 100–200 mg/d. Despite their structural similarities, the two compounds have different pharmacokinetics. Amantadine is not metabolized and is excreted almost entirely by the kidneys, with a half-life of 12–17 h and peak plasma concentrations of 0.4 μg/mL. In contrast, rimantadine is extensively metabolized to hydroxylated derivatives and has a half-life of 30 h. Only 30–40% of an orally administered dose of rimantadine is recovered in the urine. The peak plasma levels of rimantadine are approximately half those of amantadine,