CDC Revises Flu Treatment, Peramivir Guidance

BY JEFF EVANS

The Centers for Disease Control and Prevention updated its recommendations on early and late antiviral treatment during the 2009-2010 influenza season, and provided more guidance on the use of the investigational antiviral drug peramivir.

When to Start Antivirals

► **Patients with mild, uncomplicated illness who are not considered to be at increased risk of developing severe or complicated illness are not likely to benefit from antiviral treatment if started more than 48 hours after illness onset.** Similarly, patients who are already recovering from influenza do not need antiviral medications. For patients who present within 48 hours of onset, clinical judgment should be used to decide if patients with mild or uncomplicated illness and no risk factors need antiviral drugs.

► **Antiviral regimens lasting 5 days are recommended for patients with confirmed or suspected 2009 H1N1 influenza who have severe, complicated, or progressive illness, or who are hospitalized.** The 5-day treatment duration might be extended in some patients. Limited data from observational studies of hospitalized patients suggest that the initiation of antiviral treatment more than 48 hours after onset reduces mortality or duration of hospitalization in patients with prolonged or severe illness.

► **Promptly begin empiric antiviral therapy for patients with confirmed or suspected influenza who have an increased risk for complications,** the CDC advised. These include children younger than 2 years of age, children and adolescents younger than 19 years of age who are receiving long-term aspirin therapy, adults aged 65 years and older, pregnant women, and individuals with certain medical conditions (asthma; neurological and neurodevelopmental disorders; chronic lung disease; heart disease; blood, endocrine, kidney, liver, or metabolic disorders; and a weakened immune system due to disease or medication).

► **Available data suggest pregnant women should receive prompt antiviral therapy,** although no clinical studies have assessed the safety and efficacy of oseltamivir (Tamiflu) or zanamivir (Relenza) for pregnant women. The systemic activity of oseltamivir makes it the preferred treatment for pregnant women. The agency also advises prompt antiviral treatment of women up to 2 weeks postpartum with suspected or confirmed 2009 H1N1 influenza (regardless of the pregnancy outcome), because anecdotal reports have suggested that they also may be at risk for severe complications and death.

Antivirals for Vaccinated Patients

A history of vaccination does not rule out influenza, the CDC advised, because vaccination for 2009 H1N1 or seasonal influenza is effective only after 2 weeks. In addition, each vaccine is not expected to provide protection against influenza viruses other than the targeted virus. The agency recommends treating vaccinated patients as if they had not been vaccinated. People who are vaccinated with live attenuated influenza vaccines and who are given antivirals within 48 hours before or up to 2 weeks after vaccination might not develop immunity and should be revaccinated.

Oseltamivir Dosing for Infants

The CDC also updated its recommendations for dosing oseltamivir to pediatric patients. For treatment purposes, infants younger than 1 year of age should receive 3 mg/kg of the drug twice per day. For chemoprophylaxis, those aged 3 months to less than 1 year should receive 3 mg/kg oseltamivir once per day. Due to limited data, it is not recommended that the drug be given prophylactically to infants younger than 3 months unless the situation is judged to be critical. The weight-based dosing recommendations are not intended for premature infants.

Although oseltamivir dosing by weight is preferred for full-term infants younger than 1 year, it can be given according to age for treatment: 12 mg at 0-3 months, 20 mg at 3-5 months, and 25 mg at 6-11 months. Those doses should be halved for prophylaxis.

Peramivir Availability and Dosing

The Food and Drug Administration (FDA) approved the use of intravenously administered peramivir under an Emergency Use Authorization for hospitalized patients who have not responded to either oral oseltamivir or inhaled zanamivir antiviral drugs. Peramivir also is indicated when patients are expected not to have a dependable or feasible route of delivery other than intravenous, or when a clinician judges intravenous therapy to be appropriate because of other circumstances.

Pediatric patients may receive the drug if either of the first two criteria applies.

As of October, the FDA has received safety and efficacy data on the use of peramivir for 1,891 patients with acute uncomplicated seasonal influenza A. The drug has not been evaluated in hospitalized patients. It is available from the CDC upon request by a licensed physician.

The FDA now recommends that adult patients with end-stage renal disease and a creatinine clearance of less than 10 mL/minute per 1.73 m^2 who are not receiving intermittent hemodialysis or continuous renal replacement therapy should receive 100 mg of peramivir intravenously on day 1, followed by 15 mg once daily.

The updated dosing regimen for pediatric patients who have that rate of creatinine clearance but are on intermittent hemodialysis varies according to age. From birth through 30 days, infants should receive 1 mg/kg peramivir on day 1, followed by 1 mg/kg 2 hours after each hemodialysis session on hemodialysis days only. Following the same instructions, the dose increases to 1.3 mg/kg for infants 31-90 days old, 1.6 mg/kg for infants aged 91-180 days, 1.9 mg/kg for children 181 days to 5 years of age, and then back to 1.6 mg/kg for children aged 6-17 years.

Peramivir dosing for children who have a creatinine clearance of less than 10 mL/minute per 1.73 m^2 but who are not on intermittent hemodialysis or continuous renal replacement therapy follows the same initial dose on day 1 that is recommended for pediatric patients who are on intermittent hemodialysis. ■

The recommendations are available at www.flu.gov/individualfamily/prevention/medicine/antiviralsrecommend.html.