

Emergency-use authorization of peramivir

In response to the declaration of the public health emergency due to 2009 H1N1 influenza infection, FDA has authorized the first emergency-use authorization (EUA) of an investigational drug, peramivir.¹ The use of the drug must meet strict criteria, and the risk of use must be weighed against benefit. Peramivir is an injectable neuraminidase inhibitor with limited Phase II and III clinical data in approximately 1891 patients who received the drug i.v. or i.m., including 478 who received a single dose of 600 mg i.v.² Data on multiple-dose administration are limited, with 33 adult patients receiving approximately 600 mg (or more) i.v. once daily for five or more days. Limited data from clinical trials exist for treatment beyond 10 days, but patients with life-threatening infections may benefit from extended therapy. Peramivir has not been studied in pediatric and pregnant patients, and the drug is excreted into breast milk. Peramivir should be used in these populations only if the potential benefit outweighs the risk. Peramivir has demonstrated a one-day reduction in symptoms associated with H1N1 influenza, and taking the drug does not ensure the prevention of transmission of influenza to others.³

To obtain peramivir from the Centers for Disease Control and Prevention (CDC), a physician specializing in managing critically ill patients must complete an online screening form⁴ or call CDC (1-800-232-4636). Eligible patients include those with suspected or laboratory-confirmed 2009 H1N1 infection or infection due to influenza A virus not subtypable but suspected to be community circulating 2009 H1N1 virus.⁴ Adult patients for whom therapy with an i.v. medication is clinically appropriate include those (1) not responding to oral or inhaled antiviral therapy, (2) for whom drug delivery by a route other than i.v. is not expected to be dependable or feasible, and (3) for whom the clinician judges i.v. therapy appropriate due to other circumstances.⁴ Peramivir should not be used for treating infections due to uncomplicated seasonal or H1N1 influenza, or for preexposure or postexposure influenza chemoprophylaxis. For our institution, CDC approval for use of peramivir has occurred within a couple of hours of submission of the completed form. CDC contacts the hospital pharmacy listed on the screening form to ensure that the person or pharmacy identified on the form can receive delivery of the product 24 hours a

day, seven days a week. Since peramivir is not currently approved for marketing in the United States and its distribution is under the EUA, there is no charge for the drug or for its delivery.⁵ The drug is delivered within 24 hours after the order is approved.

Since peramivir is an investigational drug, institutions wanting to use it should consult their institutional review board or other entity that oversees investigational drugs, although this process is not required by CDC or FDA. FDA does require, before the initiation of therapy, that health care providers document that the patient or caregiver has (1) received the fact sheet on the drug,⁵ (2) been informed of alternatives to peramivir, and (3) been informed that peramivir is an investigational drug for use under the EUA program.

Peramivir is a clear liquid supplied as a box of five single-dose vials of 200 mg/20 mL.⁵ Detailed information on preparation and storage of the drug is included in the fact sheet for health care professionals.⁶ The standard adult dose of peramivir is 600 mg i.v. once daily for 5–10 days in patients with a creatinine clearance (CL_{cr}) of >50 mL/min.⁶ Further renal adjustments should follow the dosage recommendations in the prescribing information.⁶ Since peramivir is not extensively



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metabolized, dosage adjustment in hepatic impairment is not required.⁶

Because pediatric use of peramivir has not been studied in clinical trials, pediatric dosage is based on modeling and simulation of pharmacokinetic data from healthy adult volunteers and adult patients with influenza, patient pharmacokinetic data, and information on renal maturation and body weight.⁶ Pediatric dosage is based on age; however, for children with impaired renal function ($CL_{cr} < 49$ mL/min), dosage adjustment is calculated on the basis of CL_{cr} , age, and weight by using the Schwartz formula.⁶

Common adverse side effects include diarrhea, nausea, vomiting, and neutropenia.^{3,6} Drug monitoring should include a complete blood count with differential and basic metabolic panel on initiation, on day 3, and at the end of therapy. Liver function tests, urinalysis, renal function assessment, and vital signs should be monitored as specified in the fact sheet.⁶ Reporting through the FDA MedWatch

program⁷ of all adverse events associated with the use of peramivir is required.

1. Hamburg, MA. Letter to Frieden, TR (2009 Oct 23). www.cdc.gov/h1n1flu/eua/EUA%20Peramivir%20Letter%20-%20Frieden.pdf (accessed 2009 Nov 11).
2. Centers for Disease Control and Prevention. Clinicians considering the use of peramivir IV. <http://emergency.cdc.gov/h1n1antivirals/> (accessed 2009 Nov 11).
3. Birnkrant D, Cox E. The emergency use authorization of peramivir for treatment of 2009 H1N1 influenza. *N Engl J Med*. 2009 (10.1056/NEJMp0919479).
4. Centers for Disease Control and Prevention. Requesting peramivir IV under emergency use authorization (EUA). <http://emergency.cdc.gov/h1n1antivirals/3.asp> (accessed 2009 Nov 11).
5. Centers for Disease Control and Prevention. Emergency use authorization of peramivir fact sheet for patients and parents/caregivers. www.cdc.gov/h1n1flu/eua/Patient%20fact%20sheet%20Peramivir%20IV_23Oct2009.pdf (accessed 2009 Nov 11).
6. Centers for Disease Control and Prevention. Emergency use authorization of peramivir IV fact sheet for health care providers. www.cdc.gov/h1n1flu/eua/Patient%20fact%20sheet%20Peramivir%20IV_CDC.pdf (accessed 2009 Nov 11).

7. Food and Drug Administration. MedWatch reporting form. www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf (accessed 2009 Nov 11).

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