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FDA approves IV influenza antiviral for emergency use

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The Food and Drug Administration (FDA) has granted Emergency Use Authorization for intravenous peramivir, a neuraminidase inhibitor like oral oseltamivir (Tamiflu) and inhaled zanamivir (Relenza). Peramivir is given intravenously to treat hospitalized children with documented or suspected 2009 H1N1 influenza *who cannot tolerate* the currently licensed oral or inhaled antiviral medications. The FDA has **not** approved peramivir for *routine use* in adults or children.

There are no prospectively collected data for dosing, efficacy or safety of peramivir in children. Very preliminary data in adults suggest that the antiviral effect and safety profile of peramivir is similar to oseltamivir and zanamivir, although most of these data were collected in adults with uncomplicated influenza infections.

While substantial data are available from adults receiving a single daily dose over a range of doses from 200 mg to 600 mg, only 33 adult patients have received 600 mg doses daily for a five-day treatment course.

Complete information on how to obtain peramivir can be found on the FDA Web site (http://emergency. cdc.gov/h1n1antivirals/). Additional information, including the equivalent of a "Package Label" citing all safety and efficacy data to date, and information for parents also are available.

As one would expect, the medical community and regulatory authorities want to learn as much as possible about the safety and efficacy profile of peramivir. Therefore, the FDA reporting requirements for serious adverse events are appropriately stringent. A qualified, treating physician must document that the parents have been provided the FDA fact sheet on peramivir and told that peramivir is not an approved drug. In addition, the potential benefits of treatment must be assessed by the treating physician to be greater than any potential serious side effects.

Key points in deciding when to treat with intravenous peramivir are:

- A child must not be responding to either oral or inhaled antiviral therapy, or delivery by either an oral/nasogastric route (oseltamivir) or inhaled route (zanamivir) is NOT expected to be dependable or is not feasible.
- Dosing varies by age and renal function, with dosing instructions that are particularly critical for children with some degree of renal failure, provided in the Package Label document. The doses recommended are entirely modeled by computer simulation from adult pharmacokinetic data, with knowledge of the maturation of renal function in children from birth to adolescence.
- The side effect profile is similar to other neuraminidase inhibitors, with common adverse events including gastrointestinal symptoms (i.e., nausea, vomiting, diarrhea) or decreased neutrophil counts.
- The treatment course is five to 10 days.

The FDA also is requiring physician reporting of less common side effects, such as dizziness, headache, somnolence, nervousness, insomnia, feeling agitated, depression and nightmares, as well as suspected laboratory adverse events that may occur. Side effects are reported through the standard FDA reporting mechanism for all drug adverse events, the MedWatch program (www.fda.gov/Safety/Med Watch/default.htm).

The news of the availability of this intravenous antiviral comes none too soon for those caring for seriously ill hospitalized infants and children during this pandemic. The flexibility of the FDA to 1) release this drug for emergency use before all the usual required data are available for a full evaluation for licensure and 2) engage the medical community to responsibly provide information that will allow us to better understand this new drug highlights a partnership in which children are the clear winners.

Drs. Bradley and Bernstein are members of the AAP Committee on Infectious Diseases (COID). Dr. Bocchini is chair of COID.