

## Risk of Confusion in Dosing Tamiflu Oral Suspension in Children

**TO THE EDITOR:** The medical community should be made aware of the serious potential for dosing errors in children prescribed Tamiflu (oseltamivir) oral suspension, as illustrated in the case described below.

After the diagnosis of novel H1N1 influenza, a 6-year old received a prescription for Tamiflu (oseltamivir) oral suspension (12 mg per milliliter) at a dose of 3/4 teaspoon PO BID. However, the parents, one a primary care physician and the other one of the authors, had great difficulty determining the correct dose to administer to their child. The medication bottle was accompanied by a prepackaged syringe with markings of 30, 45, and 60 mg (Fig. 1). The label attached by the pharmacy specified the dose in volume units (“3/4 teaspoonful”) but the syringe provided only markings in mass units (milligrams). Despite the disparate directions, the parents were eventually able to determine the correct dose with the aid of 1 of 10 tables in the portion of the package insert intended for prescribers, not for parents. Specifically, they solved the following equation for the milligram equivalent of the 3/4-tsp dose:  $5 \text{ ml (volume of a teaspoon)} \times 0.75 \times 12 \text{ mg per milliliter Tamiflu suspension} = 45 \text{ mg on the syringe}$ .

Most families and caregivers would not be able to identify or perform the cumbersome calculations required to administer Tamiflu safely

to children, because the instructions on the pharmacy label, on the manufacturer’s printed label, and in the accompanying Consumer Medication Information and the prepackage dosing syringe are misaligned. Thus, there is a high chance for dosing errors, compromised treatment, or toxic effects. Even more complex dosing and measurement calculations<sup>1</sup> will be required under the Emergency Use Authorization,<sup>2</sup> which has extended the use of oseltamivir to children under the age of 1 year.

Unless immediate steps are taken to improve the prescribing instructions for this drug in children, its safe use will be compromised. We recommend that all pharmacies be instructed to ensure that the label instructions for use are in the same dosing units as those on the measurement device dispensed with oseltamivir. For instance, in the present case, the instructions could have said, “fill the attached syringe to the level marked 45 mg and administer this amount twice a day for 5 days.” If a prescription specifies the dose in teaspoons, only a syringe calibrated in fractions of a teaspoon should be dispensed and the instructions adjusted accordingly; if a prescription specifies the dose in milliliters, only a syringe calibrated in milliliters should be used. In addition, the Consumer Medication Information must be improved and the public alerted to the potential for oseltamivir dosing errors. In the future, all measuring devices for use in children should be marked with volumetric doses (milliliters or teaspoons).

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Dr. Wolf reports receiving consulting fees from Abbott and Pfizer and grant support from McNeil Pharmaceuticals, and Dr.



**Figure 1.** Tamiflu Package, Label, and Syringe Included in Box.

Wood reports being a partner and investor in Symphony Capital, serving as a director of Oxigene Pharmaceuticals, and receiving consulting fees from International Reinsurance companies. No other potential conflict of interest relevant to this letter was reported.

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- Centers for Disease Control and Prevention. Emergency use authorization of Tamiflu: fact sheet for patients and parents. July 14, 2009. (Accessed September 22, 2009, at <http://www.cdc.gov/h1n1flu/eua/pdf/tamiflu-patients.pdf>.)
- Idem*. Emergency use authorization (EUA) of medical products and devices: Tamiflu (oseltamivir). (Accessed September 22, 2009, at [http://www.cdc.gov/h1n1flu/eua/pdf/fda\\_letter\\_tamiflu.pdf](http://www.cdc.gov/h1n1flu/eua/pdf/fda_letter_tamiflu.pdf).)

**TO THE EDITOR:** On September 23, Parker et al.<sup>1</sup> described a case in which Tamiflu (oseltamivir) for oral suspension was dispensed with pharmacy instructions to administer the drug in volume units (teaspoons), whereas the manufacturer's dosing syringe accompanying the product is calibrated in milligrams. Interest in the use of oseltamivir for young children has risen since the emergence of 2009 pandemic influenza A (H1N1) virus. We recognize that dosing instructions with units different from those given on the device included with the product create risks of confusion and dosing errors.

Together, the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) have acted promptly to provide information that emphasizes appropriate dosing and dispensing of Tamiflu for oral suspension. Communications regarding potential dosing errors were posted on the CDC and FDA Web sites, and Roche has published a "Dear Healthcare Professional" letter.<sup>2</sup> All communications recommend that, when dispensing commercially manufactured Tamiflu for oral suspension, pharmacists should ensure that the units of measure on the dosing instructions match those on the device provided. If the dosing instructions specify volumetric measures (teaspoons or milliliters), the manufacturer's syringe should be removed and replaced with an appropriate device with matching units. When dispensing this suspension for children younger than 1 year of age, according to the Emergency Use Authorization, the syringe in the package should always be replaced with an appropriate measuring device, because doses for children younger than 1 year of age cannot be measured with the manufacturer's syringe.<sup>3</sup>

On September 22, the CDC posted updated

antiviral recommendations and a communication specifically for pharmacists.<sup>3</sup> The CDC disseminated this information through the Health Alert Network Information Service and other systems. The CDC also contacted pharmacists' professional organizations, associations representing drug store chains, and other retailers with pharmacies in stores to further disseminate this information widely.

On September 24, the FDA posted a Public Health Alert: "Potential Medication Errors with Tamiflu for Oral Suspension."<sup>4</sup> It reminds prescribers and pharmacists of potential errors in prescribing and dispensing Tamiflu for oral suspension in units different from those on the device in the package and recommends that providers avoid prescribing Tamiflu in teaspoons because this can lead to inaccurate dosing. The FDA also partnered with MedWatch subscribers and used social networking tools for rapid communication.

Medication-safety efforts in ambulatory settings must recognize the central role of patients and lay caregivers in medication management.<sup>5</sup> Instructions and labeling should be clear, concise, consistent, and designed for the way prescriptions are written and used. As highlighted by Parker et al., dispensing liquid medications with dosing devices with markings that match the units used in the instructions on the pharmacy label is one necessary step toward safer medication use.

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1. Parker RM, Wolf MS, Jacobson KL, Wood AJJ. Risk of confusion in dosing Tamiflu oral suspension in children. *N Engl J Med* 2009;361:1912-3.

2. Barron H. Dear Healthcare Professional letter: important prescribing information. Roche, September 23, 2009. (Accessed October 15, 2009, at <http://www.fda.gov/downloads/Safety/>

MedWatch/SafetyInformation/SafetyAlertsforHumanMedical Products/UCM183752.pdf)

3. 2009-2010 Influenza season: information for pharmacists. Atlanta: Centers for Disease Control and Prevention, 2009. (Accessed October 15, 2009, at [http://www.cdc.gov/H1N1flu/pharmacist/pharmacist\\_info.htm](http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm).)

4. FDA Public Health Alert. Potential medication errors with Tamiflu for oral suspension. Silver Spring, MD: Food and Drug Administration, 2009. (Accessed October 15, 2009, at <http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm183649.htm>.)

5. Budnitz DS, Layde PM. Outpatient drug safety: new steps in an old direction. *Pharmacoepidemiol Drug Saf* 2007;16:160-5.

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### CORRECTIONS

Long-Term Effect of Diabetes and Its Treatment on Cognitive Function (May 3, 2007;356:1842-52). In Figure 1 (page 1849), the bars for Cognitive Domain 5 should have been inverted in all three panels to show positive changes in z scores rather than negative changes. The figure has been corrected at NEJM.org.

Denosumab for Prevention of Fractures in Postmenopausal Women with Osteoporosis (August 20, 2009;361:756-65). In the Appendix (page 764), the names of some of the investigators were incomplete. The article has been corrected at NEJM.org.

DNA Damage, Aging, and Cancer (October 8, 2009;361:1475-85). In Figure 3 (page 1479), the label in the top right corner of the figure should have read "RNA polymerase" rather than "DNA polymerase." The article has been corrected at NEJM.org.

### NOTICES

Notices submitted for publication should contain a mailing address and telephone number of a contact person or department. We regret that we are unable to publish all notices received. Notices also appear on the *Journal's* Web site (NEJM.org/meetings). The listings can be viewed in their entirety or searched by location, month, or key word.

#### PUBLIC LABORATORY LOINC MEETING

The meeting will be held in Indianapolis, Dec. 7 and 8. It is jointly sponsored by the Regenstrief Institute and the National Library of Medicine.

Contact Sandy Poremba, Regenstrief Institute, 410 W. 10th St., Suite 2000, Indianapolis, IN 46202-3012; or call (317) 423-5579; or fax (317) 423-5695; or e-mail loinc-meeting@regenstrief.org; or see <http://loinc.org/meetings/20091207>.

#### INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH

The "8th Annual Meeting" will be held in San Francisco, June 16-19. Deadline for submission of abstracts is Jan. 14.

Contact the International Society for Stem Cell Research, 111 Deer Lake Rd., Suite 100, Deerfield, IL 60015; or call (847) 509-1944; or fax (847) 480-9282; or e-mail isscr@isscr.org; or see <http://www.isscr.org/>.

#### CURRENT CONTROVERSIES IN PULMONARY & CRITICAL CARE MEDICINE

The conference will be held in Carmel, CA, Jan. 29 and 30.

Contact the California Thoracic Society, American Lung Association of California (ALAC), 202 Fashion Lane, Suite 219, Tustin, CA 92780; or call (714) 730-1944; or fax (714) 730-4057; or see <http://www.thoracic.org/ca.html> or <http://www.CaliforniaLung.org>.

#### BAYLOR COLLEGE OF MEDICINE

The following course will be offered in Houston: "Psychiatry Update 2009" (Dec. 5).

Contact the Office of CME, Baylor College of Medicine, 1 Baylor Plaza, MS: BCM 155, Houston, TX 77030; or call (713) 798-8237; or fax (713) 798-7955; or e-mail cme@bcm.edu; or see <http://www.baylorcme.org/search/detail.cfm?cme=749>.

#### 8TH ANNUAL WORKSHOP ON CARDIOVASCULAR INTERVENTIONAL MRI

The workshop will be held in Orlando, FL, on Nov. 18. It is presented by the National Heart, Lung, and Blood Institute, in coordination with the American Heart Association.

Contact the National Heart, Lung, and Blood Institute, National Institutes of Health, MSC 1538, Bethesda, MD 20892-1538; or call (301) 402-6769.

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