

**From:** Clinician Outreach and Communication Activity (CDC)  
**Sent:** Wednesday, October 21, 2009 10:04 AM  
**To:** Clinician Outreach and Communication Activity (CDC)  
**Subject:** CDC Clinical Reminder: Pediatric Recommendations for the Use of Antiviral Medications: Oct 21, 2009



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In response to 2009 H1N1 Influenza, we would like to provide you with the following information. If you have any questions on these or other clinical issues, please write to us at [coca@cdc.gov](mailto:coca@cdc.gov).

**Today's topics Include:**

- [Pediatric Recommendations for the Use of Antiviral Medications](#)
- [Limited Availability of Commercially Available Tamiflu \(oseltamivir\) Suspension](#)
- [Emergency Compounding of an Oral Suspension from Tamiflu Capsules](#)
- [Resources for Patients/Parents](#)

## Pediatric Recommendations for the Use of Antiviral Medications for 2009-10 Influenza Season

Early empiric treatment with oseltamivir or zanamivir should be considered for persons with suspected or confirmed influenza who have:

- severe illness;
- evidence of clinical deterioration regardless of previous health;
- symptoms of lower respiratory tract involvement;
- illness requiring hospitalization.

In addition, early empiric outpatient treatment with oseltamivir or zanamivir should be considered for persons with suspected or confirmed influenza who are at higher risk for complications including:

- Children younger than 2 years old (Please see below for special considerations for treatment or chemoprophylaxis of children younger than 1 year old);
- Children and adolescents with certain chronic medical or immunosuppressive conditions including:
  - Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), or metabolic disorders (including diabetes mellitus);
  - Disorders that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration (e.g., cognitive dysfunction, spinal cord injuries; epilepsy, or other neuromuscular disorders);
  - Immunosuppression, including that caused by medications or by HIV;
- Pregnant adolescents and adolescents up to 2 weeks postpartum (including following pregnancy loss);
- Persons younger than 19 years old who are receiving long-term aspirin therapy, because of an increased risk for Reye syndrome;
- Children 2-4 years old are more likely to require urgent medical evaluation or hospitalization due to influenza compared with older children, although the risk is lower than for children less than 2 years old.

**Children aged 2 years to 4 years without high risk conditions (see page 3) and with mild illness do not necessarily require antiviral treatment.**

[Taken from *Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season*: <http://www.cdc.gov/h1n1flu/recommendations.htm> and from **Recommendations for Use of Antiviral Medications for the Management of Influenza in Children and Adolescent for the 2009-2010 Season - Pediatric Supplement for Health Care Providers** [http://www.cdc.gov/h1n1flu/recommendations\\_pediatic\\_supplement.htm](http://www.cdc.gov/h1n1flu/recommendations_pediatic_supplement.htm) see also the oseltamivir package insert: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2007/](http://www.accessdata.fda.gov/drugsatfda_docs/label/2007/)]

Most children and adolescents who develop a mild illness consistent with uncomplicated influenza, or appear to be recovering from influenza, do not need antiviral medications for treatment. However, clinical judgment is always an essential part of treatment decisions. Assessment of a child's or adolescent's clinical presentation and underlying risk factors for influenza-related complications and death should guide medical therapy.

## Limited Availability of Commercially Available Tamiflu (oseltamivir) Suspension

Commercial supplies of Tamiflu® oral suspension are limited. In response to this, oseltamivir oral suspension has been released from the CDC Strategic National Stockpile to enhance availability at state and local levels. This suspension product has lot numbers with expiration dates that have been extended and this product can be dispensed under the current emergency use authorization (EUA) for oseltamivir. See <http://www.cdc.gov/h1n1flu/eua/>. The extension is based on scientific testing done by the FDA, and the expiration date of the suspension can be extended beyond the date originally printed on the bottle. To check on a specific bottle's expiration date, enter the lot number at the following website to determine the extended expiration date: <http://www.cdc.gov/H1N1flu/eua/>

When local supplies of commercially-produced oral suspension are limited, physicians should consider infants and children less than one year of age or less than 33 lbs to be the highest priority for receiving the commercial suspension.

[Taken from *Recommendations for Use of Antiviral Medications for the Management of Influenza in Children and Adolescent for the 2009-2010 Season -- Pediatric Supplement for Health Care Providers*: [http://www.cdc.gov/h1n1flu/recommendations\\_pediatic\\_supplement.htm](http://www.cdc.gov/h1n1flu/recommendations_pediatic_supplement.htm)]

## Emergency Compounding of an Oral Suspension from Tamiflu Capsules

While commercially manufactured oseltamivir oral suspension (12 mg/mL) is the preferred product for pediatric and adult patients who have difficulty swallowing capsules or where lower doses are needed, this product may not be locally available.

For patients who are less than one year old or weigh less than 33 lbs (15 kg), physicians should be aware that there is one alternative:

- a suspension compounded by a retail pharmacy (see below)

For older children weighing 33 lbs (15 kg) or more there are two alternatives:

- a suspension compounded by a retail pharmacy (see below)
- 30mg, 45mg, or 75 mg capsules, which may be mixed into a sweetened liquid by a caregiver, if the child cannot swallow capsules (see below).

Oseltamivir 75 mg capsules can be compounded at most retail pharmacies into a suspension when commercially manufactured Tamiflu® oral suspension, 30mg, or 45mg capsules are not available. Health care providers can suggest this compounding alternative when writing prescriptions for oseltamivir oral suspension or capsules. Tamiflu® oral suspension concentration is **12 mg/mL**; the compounded suspension concentration is **15 mg/mL**. Compounding instructions are provided below.

Depending on the weight of the patient, if the child cannot swallow the capsules, the 30 mg, 45 mg, or 75

mg capsules can be opened and the contents mixed with a sweetened liquid such as chocolate syrup (see end of package insert at:

[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2007/021087s041\\_021246s028lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2007/021087s041_021246s028lbl.pdf)) and Questions and Answers for parents and caregivers about mixing Tamiflu® capsules for children [http://www.cdc.gov/H1N1flu/antivirals/mixing\\_tamiflu\\_qa.htm](http://www.cdc.gov/H1N1flu/antivirals/mixing_tamiflu_qa.htm)

**Compounding instructions (to be used by pharmacists/healthcare professionals) :** In the event that oseltamivir oral suspension is not available, the pharmacist may compound a suspension (15 mg/mL) from oseltamivir 75 mg capsules, using the following commercially available vehicles: Cherry Syrup (Humco®) or Ora-Sweet® SF (sugar-free) (Paddock Laboratories). Other vehicles have not been studied. First, calculate the Total Volume of an oral suspension needed to be compounded and dispensed for each patient. The Total Volume required is determined by the weight of each patient. Refer to **Table 1**.

**Table 1. Volume of an Oral Suspension (15 mg/mL) Needed to be Compounded Based Upon the Patient’s Weight**

Body Weight (kg)	Body Weight (lbs)	Total Volume to Compound per patient (mL)
≤15 kg	≤33 lbs	30 mL
16 to 23 kg	34 to 51 lbs	40 mL
24 to 40 kg	52 to 88 lbs	50 mL
≥41 kg	≥89 lbs	60 mL

Second, determine the number of capsules and the amount of vehicle (Cherry Syrup or Ora-Sweet SF) that are needed to prepare the Total Volume (calculated from Table 2: 30 mL, 40 mL, 50 mL, or 60 mL) of compounded oral suspension (15 mg/mL). Refer to **Table 2**.

**Table 2. Number of Oseltamivir 75 mg Capsules and Amount of Vehicle (Cherry Syrup OR Ora-Sweet SF) Needed to Prepare the Total Volume of a Compounded Oral Suspension (15 mg/mL)**

Total Volume of Compounded Oral Suspension needed to be Prepared	30 mL	40mL	50mL	60mL
Required number of oseltamivir 75 mg Capsules	6 capsules (450 mg oseltamivir)	8 capsules (600 mg oseltamivir)	10 capsules (750 mg oseltamivir)	12 capsules (900 mg oseltamivir)
Required volume of vehicle Cherry Syrup (Humco) OR Ora-Sweet SF (Paddock Laboratories)	29 mL	38.5 mL	48 mL	57 mL

Third, follow the procedure below for compounding the oral suspension (15 mg/mL) from oseltamivir 75 mg capsules

- Carefully separate the capsule body and cap and transfer the contents of the required number of 75 mg oseltamivir capsules into a clean mortar.
- Triturate the granules to a fine powder.
- Add one-third (1/3) of the specified amount of vehicle and triturate the powder until a uniform suspension is achieved.
- Transfer the suspension to an amber glass or amber polyethyleneterephthalate (PET) bottle. A funnel may be used to eliminate any spillage.
- Add another one-third (1/3) of the vehicle to the mortar, rinse the pestle and mortar by a triturating motion and transfer the vehicle into the bottle.
- Repeat the rinsing (Step 5) with the remainder of the vehicle.
- Close the bottle using a child-resistant cap.
- Shake well to completely dissolve the active drug and to ensure homogeneous distribution of the dissolved drug in the resulting suspension. (Note: The active drug, oseltamivir phosphate, readily dissolves in the specified vehicles. The suspension is caused by some of the inert ingredients of oseltamivir capsules which are insoluble in these vehicles.)
- Put an ancillary label on the bottle indicating "Shake Gently Before Use". [This compounded suspension should be gently shaken prior to administration to minimize the tendency for air entrapment,

particularly with the Ora-Sweet SF preparation.]

10. Instruct the parent or guardian that any remaining material following completion of therapy must be discarded by either affixing an ancillary label to the bottle or adding a statement to the pharmacy label instructions.

11. Place an appropriate expiration date label according to storage condition (see below).

**STORAGE OF THE PHARMACY-COMPOUNDED SUSPENSION:**

**Refrigeration:** Stable for 5 weeks (35 days) when stored in a refrigerator at 2° to 8°C (36° to 46°F).

**Room Temperature:** Stable for five days (5 days) when stored at room temperature, 25°C (77°F).

Note: The storage conditions are based on stability studies of compounded oral suspensions, using the above mentioned vehicles, which were placed in amber glass and amber polyethyleneterephthalate (PET) bottles. Stability studies have not been conducted with other vehicles or bottle types.

Place a pharmacy label on the bottle that includes the patient’s name, dosing instructions, and drug name and any other required information to be in compliance with all State and Federal Pharmacy Regulations. **Refer to Table 3 for the proper dosing instructions.**

**Note: This compounding procedure results in a 15 mg/mL suspension, which is different from the commercially available TAMIFLU® for Oral Suspension, which has a concentration of 12 mg/mL.**

**Table 3. Dosing Chart for Pharmacy-Compounded Suspension from oseltamivir 75 mg capsules**

Body Weight (kg)	Body Weight (lbs)	Dose (mg)	Volume per Dose 15 mg/mL	Treatment Dose (for 5 days)	Prophylaxis Dose (for 10 days)
≤15 kg	≤33 lbs	30 mg	2 mL	2 mL twice daily	2 mL once daily
16 to 23 kg	34 to 51 lbs	45 mg	3 mL	3 mL twice daily	3 mL once daily
24 to 40 kg	52 to 88 lbs	60 mg	4 mL	4 mL twice daily	4 mL once daily
≥41 kg	≥89 lbs	75 mg	5 mL	5 mL twice daily	5 mL once daily

Because infants experience high rates of morbidity and mortality from influenza, infants with 2009 H1N1 influenza virus infections may benefit from treatment using oseltamivir. Oseltamivir is authorized by the FDA for the treatment of 2009 H1N1 influenza infections in children younger than 1 year old, under an Emergency Use Authorization (see <http://www.cdc.gov/h1n1flu/eua/>).

**Table 4. Dosing recommendations for Emergency Use Authorization for antiviral treatment or chemoprophylaxis of children younger than 1 year old using oseltamivir. (Emergency Use Authorization (EUA) issued by the U.S. Food and Drug Administration (FDA), subject to the terms and conditions of the EUA. see <http://www.cdc.gov/h1n1flu/eua/>)**

Age	Recommended treatment dose for 5 days	Recommended prophylaxis dose for 10 days
Younger than 3 months	12 mg twice daily	Not recommended unless situation judged critical due to limited data on use in this age group
3-5 months	20 mg twice daily	20 mg once daily
6-11 months	25 mg twice daily	25 mg once daily

Some experts prefer weight-based dosing for children aged younger than 1 year, particularly for very young or premature infants (Based on preliminary data from a National Institutes of Health-funded Collaborative Antiviral Study Group (CASG)). If using weight-based dosing for treatment or chemoprophylaxis of infants younger than 1 year old, consider the following regimen:

- ≥ 9 months should receive 3.5 mg/kg/dose BID
- ≤ 9 months should receive 3 mg/kg/dose BID.

(D. Kimberlin et al. Oseltamivir (OST) and OST Carboxylate (CBX) Pharmacokinetics (PK) in Infants: Interim Results from a Multicenter Trial. Abstract accepted to Infectious Diseases Society of America meeting, October 2009.)

**Consider dispensing the suspension with a graduated oral syringe for measuring small amounts of suspension. If possible, mark or highlight the graduation corresponding to the appropriate dose (2 mL, 3 mL, 4 mL, or 5 mL) on the oral syringe for each patient. The dosing device dispensed with the commercially available TAMIFLU® for Oral Suspension should NOT be used with the compounded suspension since they have different concentrations.**

[Taken from Tamiflu® package insert:  
<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/>

## Resources for Patients/Parents

**Emergency Use Authorization of TAMIFLU®: Fact Sheet for Patients and Parents**  
<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM143876.pdf>

Also available in Arabic, French and Russian:  
<http://www.cdc.gov/h1n1flu/eua/tamiflu.htm>

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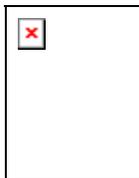
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