

Emergency Compounding of an Oral Suspension of TAMIFLU® (oseltamivir phosphate) • (Final Concentration = 15 mg/mL)



Rx only

These directions, added to the TAMIFLU package insert in November 2006, are provided for use only during emergency situations. They are not intended to be used if the FDA-approved, commercially manufactured TAMIFLU Oral Suspension is readily available from wholesalers or the manufacturer.

Commercially manufactured TAMIFLU 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.

The pharmacist may compound a suspension (15 mg/mL) from TAMIFLU Capsules 75 mg using either of two vehicles: Cherry Syrup (Humco®) or Ora-Sweet® SF (sugar-free) (Paddock Laboratories).^{*} Other vehicles have not been studied.

This compounded suspension should not be used for convenience or when the FDA-approved Tamiflu Oral Suspension is commercially available. Compounding an oral suspension with this procedure will provide one patient with enough medication for:

- a 5-day course of treatment (twice daily administration) or
- a 10-day course of prophylaxis (once daily administration).

Compounding Procedure

- 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 5. Please note that the table numbers included in these directions (Tables 5, 6, and 7) correspond to the table numbers in the TAMIFLU package insert.

Table 5: 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 or less	33 lbs or less	30 mL
16 to 23 kg	34 to 51 lbs	40 mL
24 to 40 kg	52 to 88 lbs	50 mL
41 kg or more	89 lbs or more	60 mL

^{*} Humco® is a registered trademark of Humco Holding Group, Inc.
Ora-Sweet® SF is a registered trademark of Paddock Laboratories.



Oral Dosing Device: Consider dispensing the suspension with an oral dosing device (a graduated oral syringe or spoon) suitable 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 or spoon for each patient. The dosing device dispensed with the commercially available TAMIFLU for Oral Suspension should NOT be used with the compounded suspension since it has a different concentration (concentration = 12 mg/mL) than the suspension prepared through the emergency compounding procedure described here (concentration = 15 mg/mL).

To view a video demonstration of this procedure, please go to www.RocheExchange.com.

Indications

TAMIFLU is indicated for the treatment of uncomplicated influenza caused by viruses types A and B in patients 1 year and older who have been symptomatic for no more than 2 days. TAMIFLU is also indicated for the prophylaxis of influenza in patients 1 year and older. TAMIFLU is not a substitute for early vaccination on an annual basis as recommended by the Centers for Disease Control's Advisory Committee on Immunization Practices (ACIP).

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Safety Information

There is no evidence for efficacy against any illness caused by agents other than influenza types A and B. Treatment efficacy in subjects with chronic cardiac and/or respiratory disease has not been established. No difference in the incidence of complications was observed between the treatment and placebo groups in this population. No information is available regarding treatment of influenza in patients at imminent risk of requiring hospitalization. Efficacy of TAMIFLU has not been established in immunocompromised patients.

Safety and efficacy of repeated treatment or prophylaxis courses have not been studied. In postmarketing experience, rare cases of anaphylaxis and serious skin reactions, including toxic epidermal necrolysis, Stevens-Johnson syndrome and erythema multiforme, have been reported with TAMIFLU.

There have been postmarketing reports (mostly from Japan) of self-injury and delirium with the use of TAMIFLU in patients with influenza. The reports were primarily among pediatric patients. The relative contribution of the drug to these events is not known. Patients with influenza should be closely monitored for signs of abnormal behavior throughout the treatment period.

In treatment studies in adult patients, the most frequently reported adverse events (incidence $\geq 1\%$) were nausea and vomiting. Other events reported numerically more frequently in patients taking TAMIFLU compared with placebo were bronchitis, insomnia and vertigo. In treatment studies in patients 1 to 12 years old, the most frequently reported adverse event (incidence $\geq 1\%$) was vomiting (15%). Other events reported more frequently in patients taking TAMIFLU compared with placebo included abdominal pain (5% vs 4%), epistaxis (3% vs 3%), ear disorder (2% vs 1%) and conjunctivitis (1% vs $<1\%$).

In prophylaxis studies in adult patients, adverse events were similar to those seen in the treatment studies. Events reported more frequently in patients taking TAMIFLU compared with placebo (incidence $\geq 1\%$) were nausea (7% vs 3%), vomiting (2% vs 1%), diarrhea (3% vs 2%), abdominal pain (2% vs 1%), dizziness (1% vs 1%), headache (18% vs 18%) and insomnia (1% vs 1%). In a household prophylaxis trial that included patients 1 to 12 years old, adverse events were consistent with those observed in pediatric treatment studies, with GI events being the most frequently observed.

The concurrent use of TAMIFLU with live attenuated influenza vaccine (LAIV) intranasal has not been evaluated. However, because of the potential for interference between these products, LAIV should not be administered within 2 weeks before or 48 hours after administration of TAMIFLU, unless medically indicated. Trivalent inactivated influenza vaccine can be administered at any time relative to use of TAMIFLU.

Please see accompanying complete Prescribing Information.



Pharmaceuticals

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- Next, 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 5: 30 mL, 40 mL, 50 mL, or 60 mL) of compounded oral suspension (15 mg/mL). Refer to Table 6.

Table 6: Number of TAMIFLU 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	40 mL	50 mL	60 mL
Required Number of TAMIFLU 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

- Then, follow the procedure below for compounding the oral suspension (15 mg/mL) from TAMIFLU Capsules 75 mg.



- Carefully separate the capsule body and cap and transfer the contents of the required number of TAMIFLU 75 mg Capsules into a clean mortar.

- Triturate the granules to a fine powder.

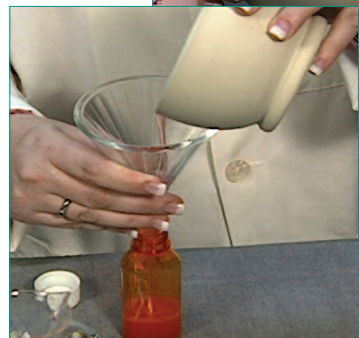
- Add one third (1/3) of the specified amount of vehicle to the mortar and triturate the powder until a uniform suspension is achieved.

- Transfer the suspension to an amber glass or amber polyethyleneterephthalate (PET) bottle. A funnel may be used to eliminate any spillage.

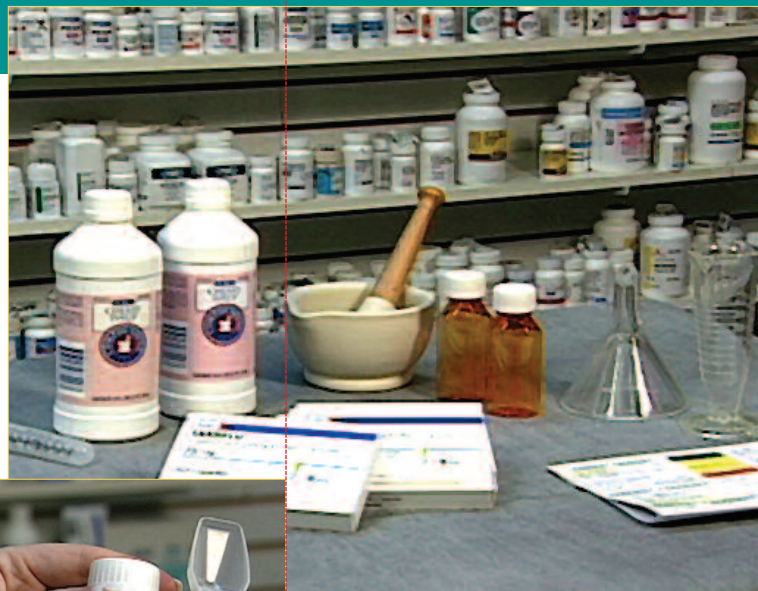
- Add another one third (1/3) of the vehicle to the mortar, rinse the pestle and mortar by a triturating motion and transfer the contents into the bottle.

- Repeat the rinsing (Step 5) with the remainder of the vehicle.

- Close the bottle using a child-resistant cap.



Tamiflu
oseltamivir phosphate
Capsules & Oral Suspension



- Shake well to completely dissolve the active drug and to insure 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 TAMIFLU 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. The need to shake the compounded oral suspension gently prior to administration should be reviewed with the patient, parent or guardian when the suspension is dispensed.

- Instruct the patient, 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.

- 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 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, drug name and any other required information to be in compliance with all State and Federal Pharmacy Regulations. Refer to Table 7 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 7: Dosing Chart for Pharmacy-Compounded Suspension from TAMIFLU Capsules 75 mg

Body Weight (kg)	Body Weight (lbs)	Dose (mg)	Volume per Dose 15 mg/mL	Treatment Dose (for 5 days)	Prophylaxis Dose (for 10 days)
5 kg or less	33 lbs or less	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 or more	89 lbs or more	75 mg	5 mL	5 mL twice daily	5 mL once daily

Note: 1 teaspoon = 5 mL.