



07 May 2009

Re: Tamiflu[®] (oseltamivir) and pharmacy compounding a suspension

The following information is related to the extemporaneous compounding of a Tamiflu suspension.

Data Sheet

The Tamiflu Data Sheet contains information on administration, on a dose-by-dose basis, of the contents of Tamiflu capsules to patients who are unable to swallow them whole.¹ There is no information in the Tamiflu Data Sheet related to the extemporaneous compounding of a Tamiflu suspension using the capsules.

However, stability data for an extemporaneously compounded solution exists and is included in this document to help the health care professional make his/her own decisions about patient care. The information provided is based on data that has not been approved by Medsafe. This should be taken into consideration before undertaking pharmacy compounding and such compounding is, therefore, the full responsibility of the pharmacist.

The Tamiflu Data Sheet is available at www.medsafe.govt.nz or www.roche.co.nz.

Compounding

Tamiflu is available as a hard gelatin capsule containing 75 mg oseltamivir. Roche recommend the administration of Tamiflu capsules according to the approved Tamiflu Data Sheet.¹

The information below is based on data generated using commercial sweetening/flavouring agents Cherry Syrup (Humco[®]) and Ora-Sweet[®] SF (sugar-free) (Paddock Laboratories).² These vehicles were chosen to allow for the development of appropriate formulations, mask the bitter taste and maximise the stability of Tamiflu capsule contents as an extemporaneous suspension. Other vehicles have not been studied. Roche are aware that Ora-Sweet[®] SF (sugar-free) is available in New Zealand through the wholesaler Health Support Limited (HSL); HSL can be contacted on 0800 70 80 60.

The following information is adapted from the US Package Insert.³

Compounding of an Oral Suspension for Patients Unable to Swallow Capsules (Final Concentration 15 mg/mL)

The following directions are provided for use only during emergency situations. Please note that Roche has not conducted clinical studies on the safety and efficacy of an extemporaneous preparation of Tamiflu. These directions are not intended to be used if the commercially manufactured Tamiflu oral suspension is readily available.

Compounding an oral suspension with this procedure will provide one patient with enough medication for a 5-day course of treatment or a 10-day course of prophylaxis for influenza.

Preparation of a Pharmacy-Compounded Suspension

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 (below).

Table 1 Volume of an oral suspension (15 mg/mL) needed to be compounded based upon the patient's weight

Body Weight (kg)	Total Volume to Compound per patient (mL)
15 kg or less	30 mL
16 to 23 kg	40 mL
24 to 40 kg	50 mL
41 kg or more	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 1: 30 mL, 40 mL, 50 mL, or 60 mL) of compounded oral suspension (15 mg/mL). Refer to Table 2 (below).

Table 2 Number of Tamiflu 75 mg Capsules and Amount of Vehicle 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 or Ora-Sweet SF)	29 mL	38.5 mL	48 mL	57 mL

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

1. Carefully separate the capsule body and cap and transfer the contents of the required number of Tamiflu 75 mg capsules into a clean mortar.
2. Triturate the granules to a fine powder.
3. Add one-third (1/3) of the specified amount of vehicle and triturate the powder until a uniform suspension is achieved.
4. Transfer the suspension to an amber glass or amber polyethyleneterephthalate (PET) bottle. A funnel may be used to eliminate any spillage.
5. 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.
6. Repeat the rinsing (Step 5) with the remainder of the vehicle.

7. Close the bottle using a child-resistant cap.
8. Shake well to completely dissolve the active ingredient and to insure homogeneous distribution of the dissolved ingredient in the resulting suspension. (Note: The active ingredient, 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.)
9. Put an ancillary label on the bottle indicating "Shake Gently Before Use". [This compounded suspension should be gently shaken prior to administration to minimise 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.

Room Temperature: Stable for 5 days when stored at room temperature, 25°C.

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.

Dosing Instructions for the Pharmacy-Compounded Suspension

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 Tamiflu capsules 75 mg

Body Weight (kg)	Dose (mg)	Volume per Dose 15 mg/mL	Treatment Dose (for 5 days)	Prophylaxis Dose (for 10 days)
15 kg or less	30 mg	2 mL	2 mL two times a day	2 mL once daily
16 to 23 kg	45 mg	3 mL	3 mL two times a day	3 mL once daily
24 to 40 kg	60 mg	4 mL	4 mL two times a day	4 mL once daily
41 kg or more	75 mg	5 mL	5 mL two times a day	5 mL once daily

Note: 1 teaspoon = 5 mL

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.

I trust that this information is helpful. Should you have any further questions, please contact the Medical Information team on 0800 276 243 if you require further assistance.

References:

1. Tamiflu® (oseltamivir) Data Sheet, 3 March 2009.
2. Winiarski AP, Infeld MH, Tscherne R, et al. Development of a stable extemporaneous preparation of oseltamivir phosphate [poster]. Presented at the American Society of Health Systems Pharmacists (ASHP), December 3-7, 2006, Anaheim, CA, USA. Poster 453.
3. Tamiflu® (oseltamivir) US Package Insert; August 2008.