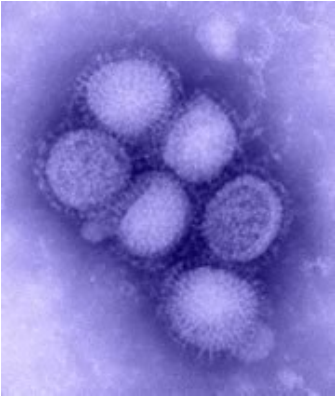


# ...Influenza, Pandemics and the Role of the Pharmacist

## Part Two - A Focus on H1N1

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### Learning Objectives:

1. Key Information about H1N1
2. How can I Protect Myself and Others from Contracting the Flu
3. Vaccination Information and Priorities
4. What can I do in the Pharmacy to Help
5. How do I Know When to Refer a Patient to a Physician?
6. Treatment and Prevention
7. How to Find Up-to-date Information Quickly
8. Summary

#### 1. About H1N1

The H1N1 virus, also referred to as the ‘swine or pig flu’ is a very contagious flu strain that is transmitted from human to human through direct contact with contaminated surfaces and the inhalation of flu droplets from an infected individual. You cannot catch H1N1 by eating pork products or through blood transfusions.<sup>1</sup>

Symptoms of H1N1 are usually of sudden onset and almost *always* include cough and fever, although fever is less prominent in young children and older adults. Other common symptoms include fatigue, muscle aches, sore throat, headache, decreased appetite, runny nose, and sometimes nausea, vomiting and diarrhea.<sup>2</sup> Shortness of breath is considered an H1N1 symptom that needs to be addressed by a physician immediately.

As of October 4, 2009, the total number of worldwide deaths associated with H1N1 was over 4500.<sup>3</sup> As of October 15, 80 of those cases occurred in Canada, 7 in Manitoba, and the virus spread in a manner consistent with the regular seasonal flu.<sup>2</sup> Although the death rate seems high, one must consider that 2,000 to 8,000 Canadians die as a result of other flu strains every year.<sup>2</sup> The usual seasonal flu targets young children and older adults whereas H1N1 targets mainly young adults. No one is exempt from the flu virus and it is imperative that people protect themselves from all types of influenza through the utilization of simple precautionary measures.

The term H1N1 reflects the name of the membrane proteins that the virus is made up of. H1N1 refers to a numbered sequence in the membrane proteins **hemagglutinin (H)** and **neuraminidase (N)**. H1, H2 and H3, as well as N1 and N2 are the strains that are associated with widespread human disease.<sup>4</sup>

H1N1 is more contagious than a typical flu and puts everyone at risk. A patient can transmit the virus from 1 day before the onset of symptoms to up to 7 days after illness onset (the regular flu is 6 days), and it's incubation period is likely 1-4 days but can be as long as 7 (the regular flu is 1-4 days).<sup>4</sup> The worst of the illness typically lasts 4 days for adults, and 3 days or less for children.<sup>5</sup> The influenza virus itself can live on hard surfaces such as stainless steel and plastic for 24-48 hours and soft surfaces such as cloth, paper and tissues for less than 8-12 hours.<sup>2</sup> However, the virus can only infect a person for up to 2-8 hours after being deposited on hard surfaces, and for up to a few minutes on soft surfaces.<sup>2</sup> It is obviously important to keep all surfaces in public areas clean and disinfected.

## **2. How can I Protect Myself and Others from Contracting the Flu?**

There are many ways that you can protect yourself and others from contracting the H1N1 flu virus as well as other types of flus and colds.

- **Wash Your Hands:** This is the single most effective way you can help to prevent the spread of disease both to yourself and to others. The proper technique of washing your hands can be found at: <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/hands-mains-eng.php#how>
- **Use Alcohol-based Hand Rubs:**
  - Follow the manufacturer's instructions
  - Your hands should be damp or slightly wet after 10-15 seconds; if they are dry, you haven't used enough product
  - The proper technique of using hand sanitizer can be found at: <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/hands-mains-eng.php#how>

**When should I wash my hands?**



- After coughing, sneezing, using a tissue
- Before preparing food, after handling raw meat
- Before and after eating
- Petting an animal
- Shaking hands or greeting people
- After using the bathroom

Teach children proper hand washing techniques and good hygiene. For additional tips see: <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/hands-mains-eng.php#how>

- **Frequent Cleaning:** clean countertops, doorknobs, light switches, telephones, and keyboards with bleach or alcohol based products to disinfect them
- **Face Masks:**
  - Controversial Issue
- **Cough and sneeze into your arm, instead of your hand**
- **Avoid touching your mouth, nose or eyes**
- **If you have flu-like symptoms, stay home until your symptoms have resolved**
- **If you are pregnant, have underlying health problems, your symptoms get worse or you have shortness of breath, contact your physician immediately**
- **Get plenty of rest**
- **Drink plenty of fluids and maintain a healthy lifestyle**
- **Be prepared:** Have on hand: Pain and fever medication to control fever and headaches, thermometer, extra supplies of medication like insulin for diabetes, cleaning supplies, soap and alcohol-based cleanser, non-perishable food such as canned soup, fruits, vegetables, water, juice in case you are sick and unable to go to the grocery store
- **Do not share:** Do not share food, drinks, stationary equipment (pens, calculators, etc.) towels, utensils
- **Get a flu shot**

### **3. The H1N1 Vaccine:**

#### ***Availability:***

The H1N1 Vaccine may be available by the time you read this article. Production was anticipated by September, tested in October, and available to the public by late October/ November, 2009. Canada contracted GlaxoSmithKline to produce 50.4 million doses of H1N1 vaccine which is enough to vaccinate all Canadians.<sup>2</sup> Health Canada has developed guidelines to assist health care providers prioritize which Canadians should be vaccinated first.

#### ***Priority Groups:***

The list in random order includes:

- People with chronic medical conditions under the age of 65.<sup>5</sup>
- Pregnant women<sup>5</sup>
- Children six months of age to under 5 years of age<sup>5</sup>
- People living in remote and isolated settings or communities<sup>5</sup>
- Health-care workers involved in pandemic response or who deliver essential health services<sup>5</sup>
- Household contacts and caregivers of individuals who are at high risk, and who cannot be immunized (such as infants under 6 months of age, or people with weakened immune systems).<sup>5</sup>

These individuals will have access to the first 7-10 million doses.

#### ***Vaccine Information:***

Vaccines work by mimicking a viral infection, leading to an immune response in the body triggering the building of antibodies against the virus. The H1N1 flu virus contains inactivated or 'killed' virus particles which consist of H1N1 antigens as well as an adjuvant system. The adjuvant may stimulate higher immune response with smaller amounts of antigen and may provide protection if drift occurs.<sup>4</sup> There will also be a non-adjuvanted vaccine available for pregnant women and children age 6 months to less than 5 years of age.<sup>6</sup> The number of vaccine doses that will be required for H1N1 is to be determined by the Government of Canada, and it can take 2 weeks until protection onset. The seasonal flu vaccine does not protect against H1N1, and an investigation is underway to determine if getting the regular seasonal flu shot increases your risk of catching H1N1.

The flu vaccine can be administered by syringe, patch or spray however, in Canada, only the intramuscular injection via syringe has been approved. The vaccine is contraindicated in people allergic to eggs and patients with a history of Guillain-Barre Syndrome.

### **4. What can I do at my Pharmacy to Help?**

Pharmacists are the most accessible health care worker available to the public, and are often the first health care professional that a patient will contact for medical advice and information. It is important to understand what role you can play and how to effectively manage the flu season.

Recommendations:

- Develop a pandemic plan with your employees
- Ensure colleagues are adhering to the prevention strategies detailed in section 2 - How to protect myself and others from contracting the flu
- If a staff member has flu-like symptoms, send them home
- When patients visit or call your pharmacy, counsel them on how to avoid and/or treat the flu
- Be on the lookout for patients asking for over the counter herbal remedies or vitamins marketed for the treatment or prevention of the cold or flu (Cold Fx, Immunity Fx, Echinacea, Vitamin C) and counsel appropriately
- Distribute patient handouts with important H1N1 flu facts and prevention strategies
- Know when to refer patients to physicians to reduce physician waiting times and unnecessary visits

## 5. How do I Know When to Refer a Patient to a Physician?

The following chart has been provided by the Canadian Pandemic (H1N1) 2009 Algorithm for use during Pandemic (H1N1) 2009 Outbreaks and is subject to change. This chart was originally designed for receptionists in physician's offices but could easily be used as a reference tool for pharmacists.

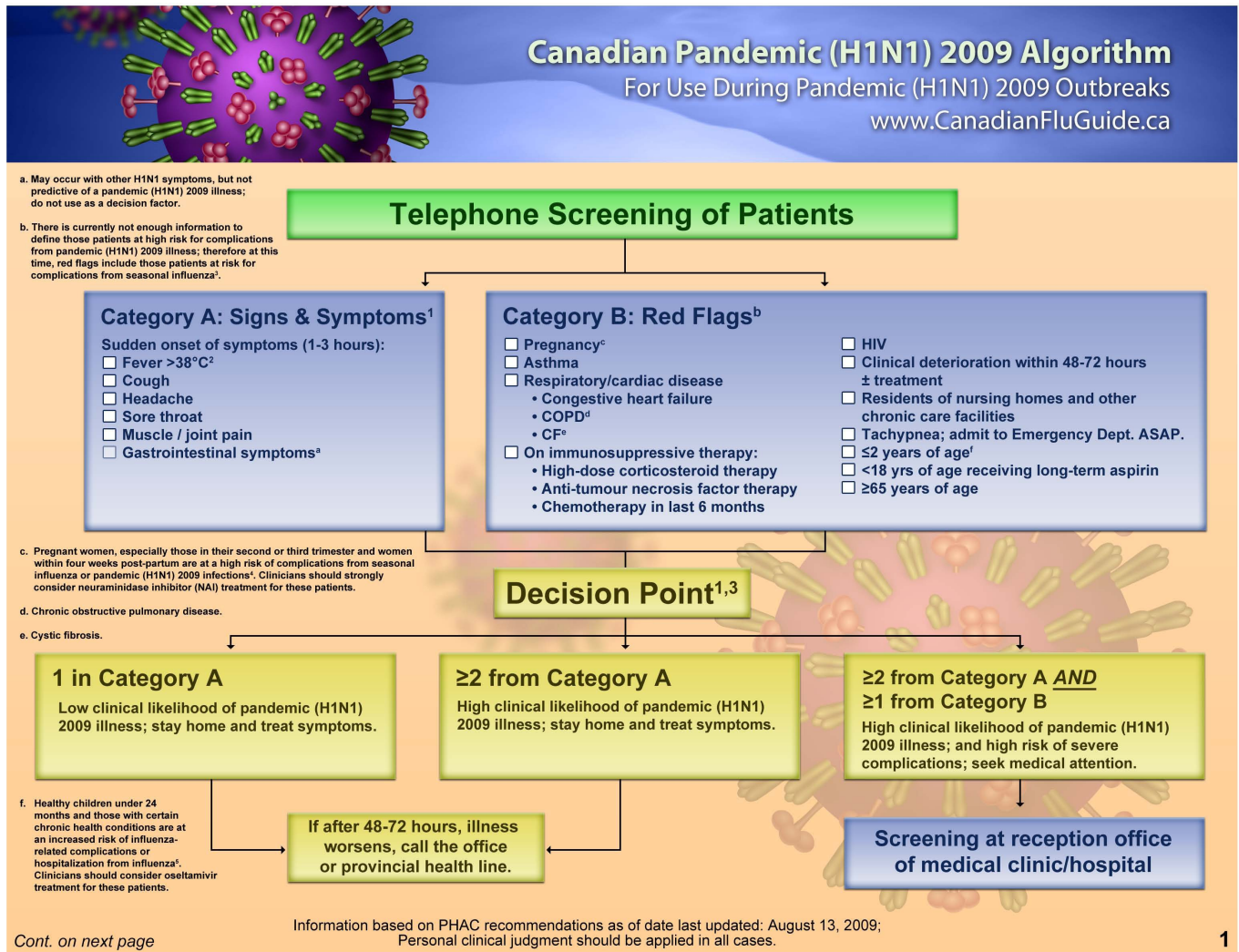


Table 1: Canadian Flu Guide: [http://www.canadianfluguide.ca/en/view.aspx?mid=H1N10101&sn=4&file=h1n1/h1n1\\_ch5\\_slides.swf](http://www.canadianfluguide.ca/en/view.aspx?mid=H1N10101&sn=4&file=h1n1/h1n1_ch5_slides.swf). Accessed Sept 28, 2009

If anyone has the following flu-like symptoms it is very important to seek medical assistance from a hospital as soon as possible as these are severe symptoms of H1N1 that need to be treated immediately: shortness of breath, rapid or difficult breathing, chest pain, asthma symptoms become worse, bluish or grey skin color, bloody or coloured mucous/spit, sudden dizziness or confusion, severe or persistent vomiting, high fever of more than 3 days, and low blood pressure. For children, signs and symptoms include the above, plus the following: a fever that isn't subsiding with medication, children who are lethargic, irritable (not wanting to play or be held), not eating/drinking, and/or not waking or interacting.

It is also very important to note that if you are a patient at high risk of developing complications from H1N1 and you develop any flu-like symptoms including mild symptoms, it is important for you to see a physician within the first 24-48 hours to start treatment immediately. Patients at high risk include Category B Red Flags, children under 5 years old, chronic

diseases, severe obesity/malnutrition, aboriginal ancestry, women within 6 weeks post-partum and conditions including smoking, substance abuse, alcoholism and homelessness.

**6. Treatment and Prevention Using Medication:**

There are only 2 medications that have been approved for the treatment and prophylaxis of H1N1:

**Oseltamivir** (Tamiflu) available in 30mg, 45mg and 75mg capsules and in powder for oral suspension, and **Zanamivir** (Relenza), circular foil disks that contain four blisters of zanamivir and lactose, for inhalation.<sup>7</sup>

**Table 2: Antiviral Options for H1N1 in Various Populations<sup>6</sup>**

| Population  | Treatment                           | Treatment Dosage           | Comments   |
|---|-------------------------------------|----------------------------|--|
| <b>Age &lt;1</b><br>(<3 months: use only if critical)   | Tamiflu x 5 days<br>(off label use) | 2mg/kg orally BID          | - Limited data; recommendations based on group's ↑'d risk for morbidity/mortality  |
| <b>Age 1-6</b>  | Tamiflu x 5 days                    | Weight                     | Dose (po)  |
|   |                                     | ≤15kg                      | 30mg BID   |
|   |                                     | >15-23kg                   | 45mg BID   |
|   |                                     | >23-40kg                   | 60mg BID   |
|   |                                     | >40kg                      | 75mg BID   |
|   |                                     |                            | <ul style="list-style-type: none"> <li>• <b>Tamiflu Commercial Powder for Suspension:</b></li> <li>- 12mg/ml (tutti frutti flavour);</li> <li>- contains 26g sorbitol; avoid if fructose intolerant</li> <li>- See Important Notes comment on</li> </ul> |
| <b>Prophylaxis:</b> Patients over 1 year of age: give same dose once daily instead of twice daily for 10 days |                                     |                            |  |
| <b>Age 7-12</b>   | Tamiflu x5 days                     | Weight based as above      |  |
|   | Relenza x5 days                     | 2 inhalations BID          |  |
| <b>Age 13-18</b>  | Tamiflu x5 days                     | 75mg BID                   |  |
|   | Relenza x5 days                     | 2 inhalations BID          |  |
| <b>Healthy Adult</b>  | Tamiflu x5 days                     | 75mg BID                   |  |
|   | Relenza x5 days                     | 2 inhalations BID          |  |
| <b>Pregnancy and Lactation</b>  | Tamiflu x5 days                     | 75mg BID                   | - Higher risk of H1N1 complications in 3 <sup>rd</sup> trimester   |
|   | Relenza x5 days                     | 2 inhalations BID          | - Higher risk of H1N1 through 4 weeks post-partum  |
|   |                                     |                            | - Tamiflu preferred: more data & ?fetal protection   |
|   |                                     |                            | - Relenza: less systemic absorption; limited data  |
| <b>COPD/Asthma</b>  | Tamiflu x5 days                     | 75mg BID                   | - Relenza has been known to cause bronchospasm   |
| <b>Renal Impairment</b>   | Tamiflu x5 days                     | CrCl: 10-30mL/min: 75mg OD | - No dose adjustment required for Relenza, 10-20% may be absorbed;   |

|   |                 |  |  |
|---|-----------------|--|--|
|   |                 | CrCl: <10mL/min: AVOID   | therefore monitor for systemic adverse effects (e.g. behavioural, suicide)                   |
| <b>Critically III/ICU</b><br><br>-severe, progressive disease | Relenza x5 days | 2 inhalations BID  |  |
|   | Tamiflu x5+days | 75-150mg BID <sup>WHO 10</sup><br>(depending on weight; renal function permitting) | - Consider extending the treatment duration &/or ↑ dosage to 150mg BID (especially if obese) |
|   | Relenza x5 days | 2 inhalations BID  | - NOT for nebulizer/ventilator mechanical, not for reconstitution                            |

Table 2: Rx Files. Influenza Overview 2009: With Consideration for Pandemic H1N1. Accessed October 13, 2009. Slightly modified October 13, 2009.

### Important Notes:

#### Tamiflu:

##### - Suspension Dosing Errors:

- Oral dosing dispenser with 30mg, 45mg and 60mg graduations has resulted in errors if directions given in mL or teaspoons.<sup>6</sup> Ensure units of measure in dosing instructions match those on the device given. Order in 'mg'!<sup>6</sup>
- Please visit <http://www.tamiflu.com/hcp/dosing/extprep.aspx> , or the CPS for Compounding Tamiflu Oral Suspension from Tamiflu Capsules
- Prophylaxis for ages 13 and older is treatment with Tamiflu 75mg once daily for 10 days. Treatment should be started within 2 days of exposure.
- Concerns about resistance if overused.<sup>6</sup>
- Drug interactions: clinical significance unknown, but clopidogrel may ↓ Tamiflu metabolism/effect, Probenacid may ↑ Tamiflu levels, methotrexate may interact.<sup>6</sup>
- Side effects include nausea and vomiting 10%. Rare: behaviour changes especially with kids.<sup>6</sup>
- Oseltamivir reduces the median time to symptom resolution of 20.69 hours (0.9 days) for otherwise health adults.<sup>7</sup>
- Data from the IMPACT study (which studied patients during the 1999-2000



influenza season) shows that patients experienced a shorter duration of illness the earlier treatment was started with oseltamivir.<sup>7</sup> Data from the IMPACT study showed that, if treated within 12 hours of the onset of symptoms (rather than at 48 hours), the median duration of illness was reduced by nearly 3.1 days.<sup>7</sup>

#### Relenza:

- Relenza treatment is usually 2 inhalations stat; repeat after 2 hours, then 2 inhalations every 12 hours.<sup>6</sup>
- Side effects include nasal/throat irritation, headache, nausea, cough; very rare: behaviour changes especially in kids.<sup>6</sup>
- Should not be used in those with severe underlying airway disease such as asthma or COPD.<sup>6</sup>
- Prophylaxis with Relenza is once daily inhalation x10+ days.<sup>6</sup>

- Zanamivir treatment reduces the median time to alleviation of symptoms as compared to placebo, by 0.8 days.<sup>7</sup>

### **In General:**

- Prophylaxis is not routinely recommended, even if a member of your family has the H1N1 flu. Prophylaxis is recommended for residents and staff of closed care facilities, and close contacts of cases at high-risk for contracting severe disease.<sup>7</sup>
- Treatment is indicated only for those who are at high risk of developing complications from the H1N1 virus (Category B in the Telephone screening tool).
- Patients who require lab confirmation of H1N1 include patients who require hospitalization, pregnant women, or index cases.
- **Tamiflu and Relenza are not wonder drugs!!! They really only reduce the duration of symptoms for 1 day, so prevention is key!!!**

### **Calculation of Creatinine Clearance (ml/min) (for ADULTS ≥18 years ONLY):**

**Cockcroft and Gault equation:**

$$\text{CrCl} = (140 - \text{age}) \times \text{IBW} / (\text{Scr} \times 72) \quad (\times 0.85 \text{ for females})$$

**Calculator:**

<http://www.globalrph.com/crcl.htm>

**Estimate Ideal body weight (IBW) (kg)**

Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet.

Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet.

**MDRD study equation:**

$$\text{GFR (mL/min/1.73 m}^2\text{)} = 175 \times (\text{S}_{\text{cr}}/88.4)^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American}) \text{ (SI units). The Scr is in units of } \mu\text{mol/L.}$$

**Calculator:**

[http://www.nkdep.nih.gov/professionals/gfr\\_calculators/idms\\_si.htm](http://www.nkdep.nih.gov/professionals/gfr_calculators/idms_si.htm)

**For children up to the age of 18 (for both equations) a different equation is used and a web calculator can be found at the following link:**

[http://www.kidney.org/professionals/kdoqi/gfr\\_calculatorPed.cfm](http://www.kidney.org/professionals/kdoqi/gfr_calculatorPed.cfm)

It is important to keep in mind when figuring out the Creatinine Clearance that there are limitations to using these equations. The limitation of these equations include: adults (>18 years of age); the equations are only valid if renal function is stable; the equations are not validated in patients with “markedly abnormal body composition” (e.g. extreme obesity, cachexia, paralysis, amputation, pregnancy); estimations may also be inaccurate in patients following vegetarian diets, taking creatine supplements, or taking medications that inhibit the tubular secretion of creatinine (eg. trimethoprim).<sup>12</sup>

A 24 hour glomerular filtration rate may have to be used in certain situations including extremes of age and body size, severe malnutrition or obesity, disease of skeletal muscle, paraplegia or quadriplegia, vegetarian diets, rapidly changing renal function, and pregnancy.<sup>12</sup>

It is also important to note that using these equations are just guidelines and that patients need to be monitored for their response to medications, and doses should be altered according to patient response.

### **7. How to Find Up-to-date Information Quickly :**

1.) Public Health Contact Information:

Manitoba: 1-800-782-2437 [www.gov.mb.ca/health/index.html](http://www.gov.mb.ca/health/index.html)

2.) H1N1 Flu Hotline: 1-800-454-8302

3.) The Canadian Flu Guide: [www.CanadianFluGuide.ca](http://www.CanadianFluGuide.ca)

4.) Health Canada website: [http://www.phac-aspc.gc.ca/alert-alerte/h1n1/faq\\_rg\\_h1n1-eng.php](http://www.phac-aspc.gc.ca/alert-alerte/h1n1/faq_rg_h1n1-eng.php)

- 5.) Centers for Disease Control and Prevention: <http://www.cdc.gov/H1N1FLU/>
- 6.) Public Health Agency of Canada: <http://www.phac-aspc.gc.ca/alert-alerte/h1n1/surveillance-eng.php>
- 7.) MPhA H1N1 Flu Information site: <http://napra.ca/pages/Manitoba/default.aspx?id=2411>
- 8.) Manitoba Health H1N1 Flu Information site: <http://www.manitoba.ca/flu/index.html>
- 9.) The Canadian Pharmacists Association: Pandemic Influenza: A guide for Pharmacists in Pandemic Preparedness.  
[http://www.pharmacists.ca/content/hcp/resource\\_centre/practice\\_resources/pandemic2.cfm](http://www.pharmacists.ca/content/hcp/resource_centre/practice_resources/pandemic2.cfm)
- 10.) **How to Prepare a Tamiflu Suspension:** <http://www.tamiflu.com/hcp/dosing/extprep.aspx>

## 8. Summary

Pharmacists must educate staff and patients about the best approaches to staying healthy, vaccine information, treatment strategies, and when a patient must be referred to a physician. Familiarize yourself with antiviral medications and resources that will help you locate up-to date information quickly. Pharmacists have an opportunity to play a critical role managing this flu season and a potential H1N1 pandemic ; are you ready?

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**Disclaimer:** The contents of this article were written in September and October, 2009 and information is subject to change. H1N1 information changes on a daily basis. The writer and the writer's affiliates are not responsible for outdated information that may become inaccurate over time. Please refer to the Great Resources area of the article for updated information, including the Public Health Agency of Canada and Health Canada.

## How to Prepare Tamiflu Suspension from Capsules

This information was taken word for word from the Tamiflu Monograph located at

<http://www.tamiflu.com/hcp/dosing/extprep.aspx>

Directions for the Emergency Compounding of an Oral Suspension from TAMIFLU Capsules (Final Concentration = 15 mg/mL) <sup>1</sup>

In November 2006, the FDA approved the addition of directions for the emergency compounding of a TAMIFLU oral suspension from TAMIFLU Capsules (15 mg/mL) to the label. These directions 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

In the event that the commercially manufactured TAMIFLU Oral Suspension is not available, the pharmacist may compound a suspension (15 mg/mL) from TAMIFLU (oseltamivir phosphate) Capsules 75 mg using either of two vehicles: Cherry Syrup (Humco®)\* or Ora-Sweet® SF (sugar-free).

† 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 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 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                                     |

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<br>Cherry Syrup (Humco) OR<br>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

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 to the mortar 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 contents 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 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.)
9. 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 parent or guardian when the suspension is dispensed.*
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.

12. 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 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) |
|------------------|-------------------|-----------|--------------------------|-----------------------------|--------------------------------|
| 15 kg or less    | 33 lbs or less    | 30 mg     | 2 mL                     | 2 mL two times a day        | 2 mL once daily                |
| 16 to 23 kg      | 34 to 51 lbs      | 45 mg     | 3 mL                     | 3 mL two times a day        | 3 mL once daily                |
| 24 to 40 kg      | 52 to 88 lbs      | 60 mg     | 4 mL                     | 4 mL two times a day        | 4 mL once daily                |
| 41 kg or more    | 89 lbs or more    | 75 mg     | 5 mL                     | 5 mL two times a day        | 5 mL once daily                |

Note: 1 teaspoon = 5 mL

*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).**

This completes the review of the directions for the emergency compounding of an oral suspension of TAMIFLU from the oral 75 mg capsules. Healthcare professionals should access the TAMIFLU Package Insert, which contains these directions and all tables needed to complete the emergency compounding procedure.