

Guidelines for the use of Oseltamivir in Long Term Care Facilities

Purpose

To provide guidance to infection control professionals, prescribers and medical directors of long term care (LTC) facilities and personal care homes (PCH) on the use of oseltamivir for treatment and prophylaxis of influenza before and during outbreaks. **Routine use of antiviral prophylaxis of asymptomatic contacts outside an institutional outbreak is not recommended.**

It is recommended to monitor the seasonal influenza surveillance reports for strain circulation, vaccine-strain match and antiviral resistance.

- [Provincial Respiratory Surveillance Report](#)
- [Canada \(FluWatch\)](#)

Oseltamivir (Tamiflu®)

Mechanism of Action

- Neuraminidase inhibitor (NAI) – virion release from infected cells and spread within the respiratory tract are inhibited due to blockade of this enzyme
- Shown to reduce hospitalization and mortality in high-risk patients with seasonal or pandemic influenza (Aoki et al., 2019)
- Influenza B viruses are less susceptible (10-20 fold) to oseltamivir than influenza A viruses so oseltamivir treatment may be less effective against influenza B viruses (Aoki et al., 2019)
- Influenza resistance to oseltamivir remains rare
 - In the 2019-2020 influenza season, 99.6% of influenza A (H1N1) viruses tested were sensitive to oseltamivir (PHAC, 2021). One virus was resistant to oseltamivir with the H275Y mutation in the neuraminidase gene.
 - During the 2021–2022, 259 influenza viruses (246 A(H3N2) and 11 A(H1N1)) were tested for antiviral resistance, with 100% of viruses sensitive to each oseltamivir (Buckrell et al., 2022).

Health Canada Approved Indications

- Treatment of uncomplicated influenza A and B in patients 1 year of age or older who have been symptomatic for no more than 2 days
- Prevention of influenza A and B in adults and children 1 year of age and older who are close contacts of an individual with characteristic symptoms of influenza

Pharmacokinetics

- Absorption: Well absorbed
- Metabolism: Extensively converted (90%) in the liver to oseltamivir carboxylate (active antiviral molecule)
 - Little potential for drug-drug interactions
 - No dose adjustment required for obese adults or people with mild or moderate hepatic impairment
- Excretion: Urine by glomerular filtration and renal tubular secretion (greater than 90%)
 - Dose reduction required for creatinine clearance less than 30 mL/min

Adult Dosing

- In preparation for influenza season, each PCH/LTC site should populate [LTC Oseltamivir Dosing Spreadsheet](#) with the resident demographic information and serum creatinine values.
 - The spreadsheet will calculate the resident's creatinine clearance and appropriate oseltamivir treatment and prophylaxis dosing
 - In the event of an influenza outbreak, the spreadsheet also calculates the number of boxes of oseltamivir 30 mg and 75 mg to order from MDA
 - The spreadsheet should be reviewed at least monthly during influenza season and updated with any resident moves, admission, deaths, or updated serum creatinine values

Creatinine Clearance	Treatment for 5 days	Prophylaxis for 10 days or until the outbreak is over, whichever occurs first
Greater than 60 mL/min	75 mg po twice daily	75 mg po once daily
Greater than 30 up to 60 mL/min	75 mg po once daily	30 mg po once daily
10-30 mL/min	30 mg po once daily	30 mg po every other day
Less than 10 mL/min or dialysis	Consult the Manitoba Renal Program or Infectious Diseases	

Treatment

- **Initiate oseltamivir treatment immediately** for LTC/PCH residents with signs and symptoms of influenza-like illness (ILI). The ILI case definition is outlined in Table 1 of the [Shared Health Manitoba Infection Prevention and Control Outbreak Management Guidelines](#).

TABLE 1: INFLUENZA-LIKE ILLNESS

ILI Case Definition	<p>Acute onset of respiratory illness with fever AND cough and with one or more of the following:</p> <ul style="list-style-type: none"> • Sore throat • Arthralgia (joint pain) • Myalgia (muscular pain) • Prostration (extreme exhaustion) that could be due to influenza <p>In children < 5 years of age, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea) may be present.</p> <p>In patients < 5 years or ≥ 65 years old, fever may not be prominent.</p>
	<p>NOTE: Illness associated with novel influenza viruses may present with other symptoms</p> <p>Source: MH Seasonal Influenza protocol (gov.mb.ca)</p> <p>NOTE FOR LTC SETTINGS:</p> <ol style="list-style-type: none"> 1. fever definition is single oral temperature >37.8°C or 2. Repeated oral temperatures >37.2°C or rectal temperatures >37.5°C or 3. Single temperature >1.1°C over baseline from any site (oral, tympanic, auxiliary). <p>Source for Fever Definition: Infection Prevention and Control Canada (IPAC Canada), Can J Infect Control, Fall 2017 (Suppl):10-17.</p>

- Treatment should be initiated as rapidly as possible after onset of illness because the benefits of treatment are much greater with initiation at less than 12 hours than with initiation at 48 hours (Aoki et al., 2019)
- Starting treatment within 12 hours of illness onset is a practice goal (Aoki et al., 2019)
- Since people of any age who are residents of nursing homes or other chronic care facilities are identified as a group at high risk for severe disease, antiviral therapy should be initiated even if the interval between illness onset and administration of antiviral medication exceeds 48 hours (Aoki et al., 2019)
- Higher doses of oseltamivir cause more adverse events and offer no benefit over the standard doses outlined above (Aoki et al., 2019)
- Oseltamivir treatment duration is 5 days but may be continued longer for severely ill individuals in consultation with infectious diseases
- If the nucleic acid amplification test (NAAT) for influenza is negative, discontinue oseltamivir treatment (Mubareka et al., 2020)
- If a resident is not responding to oseltamivir treatment,
 - Consider bacterial coinfection in residents with suspected or laboratory-confirmed influenza who:
 - Present with severe disease (e.g., extensive pneumonia, respiratory failure, hypotension, and fever)
 - Deteriorate after initial improvement
 - Fail to improve after 3-5 days of antiviral treatment (Uyeki et al., 2019)
 - Consider oseltamivir resistance in consultation with Infectious Diseases

Prophylaxis

- To control outbreaks in closed facilities, antiviral prophylaxis, combined with treatment and inactivated vaccine administration, is indicated (Aoki et al., 2019)
- **Immediately upon lab confirmation of a confirmed influenza case:**
 - Follow the [Influenza Outbreak Management QUICK REFERENCE GUIDE for LTC IP&C](#) and [Shared Health Manitoba Infection Prevention and Control Outbreak Management Guidelines](#) regarding outbreak declaration.
 - Once outbreak has been confirmed with regional IP&C, contact the site Medical Director regarding approval for oseltamivir prophylaxis.
 - Per the [Manitoba Health Seasonal Influenza Communicable Disease Management Protocol](#), when an outbreak has been declared, unless contraindicated, antiviral prophylaxis is recommended for all residents regardless of influenza vaccination history, who have not already been ill with ILI
 - If further medical consultation is required, the site Medical Director can contact the IP&C Medical Director (Dr. John Embil or designate)
 - Antiviral prophylaxis for health care workers should be discussed with Occupational Health (if available) or referred to their primary care provider
 - If the outbreak is not over after 10 days, the site Medical Director should consult the IP&C Medical Director (Dr. John Embil or designate) to see if oseltamivir prophylaxis should continue
- A prescriber order for oseltamivir prophylaxis during an influenza outbreak is included in the *PCH Medication Standing Orders* and can be initiated if:
 - 1) An influenza outbreak has been declared in discussion with regional IP&C
AND
 - 2) Oseltamivir prophylaxis is approved by the PCH/LTC Medical Director or MOH
AND
 - 3) The resident is asymptomatic and has not already been ill with ILI

Adverse Effects

- Generally, well tolerated
- Gastrointestinal
 - Most common after the first dose and tends to improve with subsequent dosing
 - Administration with meals may improve gastrointestinal tolerability
 - Nausea (4-10%)
 - Vomiting (2-15%)
 - Abdominal pain (2-5%)
 - Diarrhea (1-3%)
- Headache
- Skin rashes

Oseltamivir Supply

- **BEFORE a confirmed influenza outbreak**
 - A resident-specific order for oseltamivir treatment should be obtained from the prescriber for residents with ILI symptoms (see definition under “Treatment” above)
 - **Give the first dose of oseltamivir without delay from the PCH stat box**
 - The stat box within each PCH should contain oseltamivir 30 mg and oseltamivir 75 mg capsules (minimum 5 capsules; maximum 10 capsules)
 - The current stat box supply and expiry date should be checked each August and then at least monthly throughout the influenza season (Oct-Apr)
 - If resident ILI illness cases are suspected, more frequent monitoring of oseltamivir supply (at least weekly) should occur. Reorder from pharmacy, as required.
 - Fax the resident-specific oseltamivir order to the pharmacy. Oseltamivir is covered by the PCH Drug Benefit List
 - Pharmacy will supply the remaining doses in the 5-day oseltamivir treatment course

- Continue to give the resident their oseltamivir doses from the stat box until the resident-specific supply arrives from pharmacy
- **AFTER confirmation of an influenza outbreak**
 - Contact the site Medical Director to approve oseltamivir prophylaxis and which residents to include
 - Ensure the *LTC Oseltamivir Dosing spreadsheet* is current which will calculate how many boxes of oseltamivir 75 mg (10 capsules/box) and how many boxes of oseltamivir 30 mg (10 capsules/box) are required. The unit-specific filter worksheet can be used if ordering for one or more units instead of the whole facility. **Do not order excess amounts of oseltamivir as it cannot be returned.**
 - Order oseltamivir as soon as possible from Materials Distribution Agency (MDA Provincial Warehouse) at (204) 948-1333 (regular hours) or (204) 805-4096 (after hours)
 - Provide the following information:
 - PCH name
 - Lab confirmed organism implicated in the outbreak
 - Name of the site Medical Director or Manitoba Health Officer (MOH) who approved the oseltamivir prophylaxis
 - Number of boxes of each oseltamivir 30 mg and 75 mg required
 - Contact person at the PCH and phone #
 - Delivery instructions (e.g., delivery address, entrance, cell phone number, buzzer, door code, etc..)
 - Request oseltamivir delivery as soon as possible
 - If new residents develop ILI illness symptoms, a resident-specific order should be obtained from the prescriber to switch the resident to treatment dosing. Additional oseltamivir may be required from MDA to complete their course.

Administration

- Transcribe oseltamivir orders on to the resident's medication administration record (MAR):
 - For treatment dosing, transcribe the oseltamivir prescriber order by hand in the next blank space on the MAR
 - For prophylaxis dosing, it is recommended to use the oseltamivir prophylaxis dosing labels to transcribe the oseltamivir prophylaxis standing order in the next blank space on the MAR. The label templates are available for download and printing at these links:
 - CrCl greater than 60 mL/min – 75 mg once daily
 - CrCl greater than 30 mL/min up to 60 mL/min – 30 mg once daily
 - CrCl 10-30 mL/min – 30 mg po every other day
- When the oseltamivir supply arrives from MDA:
 - Assign one oseltamivir box (10 doses/box) per resident receiving treatment (if not already received from pharmacy) or prophylaxis. This will permit monitoring of the number of doses the resident has received
 - Label the oseltamivir box with the resident's identifiers using a resident chart label or addressograph label
 - Store the oseltamivir box in the resident's pouch porter in the medication cart, if space permits

Approach to Mixed Influenza and COVID-19 Outbreak

Use of oseltamivir prophylaxis in PCHs that meet the criteria for an influenza outbreak, and have both influenza and COVID-19 detected among the symptomatic residents:

- Asymptomatic residents:
 - Initiate oseltamivir prophylaxis for asymptomatic residents using the PCH Medication Standing Orders
- Symptomatic residents meeting the definition of ILI (see Table 1):
 - [Submit an NP swab for PCR testing](#)
 - [While awaiting the PCR results, contact the resident's prescriber for an order for oseltamivir treatment](#)
 - [If influenza is identified, complete oseltamivir treatment course](#)
 - [If influenza is NOT identified, contact the resident's prescriber to change oseltamivir dosing to prophylaxis](#)

- If COVID-19 is identified, review if resident is eligible for COVID-19 antiviral
- There are no concerns with coadministration of a COVID-19 antiviral and oseltamivir for influenza prophylaxis

References

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