Prescriber Guidelines for the use of Oseltamivir in Long Term Care Facilities within the Winnipeg Health Region

Purpose
To provide guidance to the Medical Directors of long term care (LTC) facilities on the use of oseltamivir for treatment and prophylaxis of Influenza before and during outbreaks. Routine use of antiviral chemoprophylaxis of asymptomatic contacts outside an institutional outbreak is not recommended.

It is recommended to follow the seasonal influenza surveillance reports circulated during the season on trends, strain circulation and vaccine strain match. This could be found at: http://www.gov.mb.ca/health/publichealth/surveillance/influenza/index.html

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
- Resistance – Rare instances of infection with oseltamivir-resistant 2009 H1N1 virus strains have been reported; >99% of influenza viruses circulating since September 2009 have been sensitive to oseltamivir

Health Canada Approved Indications
- Treatment of uncomplicated influenza A and B in patient 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 which 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
- Excretion: Urine by glomerular filtration and renal tubular secretion (>90%)
  - Dose reduction required for creatinine clearance less than 30 mL/min

Dosing

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Treatment for 5 days</th>
<th>Prophylaxis until outbreak is over</th>
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<tbody>
<tr>
<td>Greater than 60 mL/min</td>
<td>75 mg po twice daily</td>
<td>75 mg po once daily</td>
</tr>
<tr>
<td>Greater than 30 up to 60 mL/min</td>
<td>75 mg po once daily</td>
<td>30 mg po once daily</td>
</tr>
<tr>
<td>10-30 mL/min</td>
<td>30 mg po once daily</td>
<td>30 mg po every other day</td>
</tr>
<tr>
<td>Less than 10 mL/min or dialysis</td>
<td>Consult the Manitoba Renal Program or Infectious Diseases</td>
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Adverse Effects
- Generally well tolerated
- Gastrointestinal
  - Nausea (4-10%)
    - Most common after the first dose and tends to improve with subsequent dosing or taking with food
  - Vomiting (2-15%)
  - Abdominal pain (2-5%)
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Approved by the LTC Medical Director Advisory Council – November 19, 2015

- Diarrhea (1-3%)
  - Headache
  - Skin rashes

Supply
- Oseltamivir for treatment of residents with influenza-like illness outside of an outbreak can be obtained from the pharmacy. It is covered by the PCH Drug Benefit List.
- The stat box within the PCH should contain 1 box of oseltamivir 30 mg and 1 box of oseltamivir 75 mg available at all times so treatment can begin without delay.
- Oseltamivir 30 mg and 75 mg capsules for treatment or prophylaxis during an outbreak is obtained from the Manitoba Provincial Warehouse.

References
3. Dr. Bunmi Fatoye, Draft Operational Guidelines for Oseltamivir Prophylaxis.

Procedure / Process

Prior to a lab confirmation of influenza illness in a facility, infection prevention and control measures should already be in place. Refer to the regional management of influenza in LTC facilities available at: http://www.wrha.mb.ca/extranet/ipc/manuals-ltc-sec10.php

The decision to initiate prophylaxis can be made immediately upon confirmation of Influenza as the causative organism early on in the outbreak.

1. Review of outbreak curve. This will be provided by your infection prevention and control professional or designate
   - What is the progression over time?
     - Number of cases increasing daily signals ongoing transmission
     - Is the slope of the curve on the rise or at peak?
     - When was the last new case reported? If there are no cases approximately 4 days since last case i.e. one period of communicability, this may signal reduced transmission
   - Who is affected – residents only, staff only or both residents and staff. This provides some indication on how wide spread the Influenza is.
   - What is the attack rate in the facility?

2. What is the degree of severity?
- Mild – ILI (Influenza-like Illness) symptoms with no shortness of breath and no change in chronic condition
- Moderate - ILI symptoms with respiratory distress – shortness of breath, and change in chronic condition
- Severe - Pneumonia or other complications requiring hospitalization
- What is the number requiring hospitalization or number of deaths?

3. Is the outbreak localized in one or multiple units within the facility?
   - If cases are occurring in multiple locations in the facility and there is no illness in staff, there is an assumption that the vehicle of transmission could be staff or visitors. This could also be interpreted as staff not reporting illness; are staff truly not ill, or are they experiencing subclinical infection, or there is no active staff surveillance taking place?
   - If cases are localized in one unit and there is IP & C measures in place, oseltamivir could be initiated for that unit only in situations of low severity.

4. What infection prevention measures are implemented in the whole facility? How feasible is the cohorting of ill residents and staff within the facility?

5. What is the vaccine coverage rate for residents and staff? Low coverage might indicate the need for prophylaxis in a good match season with a high attack rate.

6. What is the vaccine-strain match? Poor match will create a low threshold for initiation of prophylaxis.

7. Influenza B is less virulent in elderly population and causes a milder disease than type A - it primarily affects children. There have been studies suggesting less susceptibility to oseltamivir i.e. reduced clinical efficacy compared to influenza A. Influenza B occurs later in the season. Evaluation of the use of oseltamivir during outbreaks should be done on an incident by incident basis taken into consideration the above points.

8. Medical Directors may consult with the Medical Officer of Health as the need arises on a facility by facility basis.
Adult resident of a long term care facility develops signs/symptoms of influenza-like illness (ILI)

Does the resident have moderate, progressive or severe complicated illness?

Mild or uncomplicated illness

Was the onset of symptoms less than 48 hours?

YES

YES

Consider hospitalization if illness cannot be managed onsite

NO

NO

Presence of risk factors for progression to severe disease*

Consider oseltamivir treatment

Initiate oseltamivir treatment immediately even if the interval between symptom onset and initiation is longer than 48 hours

Initiate oseltamivir treatment immediately

*Risk factors for progression to severe disease include: Asthma and other chronic pulmonary disease including bronchopulmonary dysplasia, cystic fibrosis, chronic bronchitis and emphysema; Cardiovascular disease (excluding isolated hypertension; including congenital and acquired heart disease such as CHF and symptomatic CAD); Malignancy; Chronic renal insufficiency; Diabetes mellitus and other metabolic diseases; Hemoglobinopathies such as sickle cell disease, immunosuppression or immunodeficiency (e.g., HIV infection, especially if CD4 is <200x10^6/L), or iatrogenic, due to medication; Neurologic disease and neurodevelopmental disorders that compromise handling of respiratory secretions (cognitive dysfunction, spinal cord injury, seizure disorders, neuromuscular disorders, cerebral palsy, metabolic disorders); Individuals 65 years of age and older; people of any age who are residents of nursing homes or other chronic care facilities; pregnant women and women up to 4 weeks post-partum regardless of how the pregnancy ended, obesity with a BMI>40 or a BMI>3 z scores above the mean for age and gender, aboriginal peoples.
**INFLUENZA-LIKE ILLNESS OUTBREAK IN A LONG TERM CARE FACILITY**

2 or more ILI cases in the same facility unit/area within 7 days

Is there a laboratory confirmed Influenza A or B in at least one of the ILI cases?

- **NO**
  - Rapid tests are negative and PCR test results are pending

  - **NO**
    - PCR results return within 24 hours?
      - **NO**
        - Is there a vaccine mismatch or more virulent Influenza strain?
          - **NO**
          - Continue with outbreak management excluding prophylaxis
          - **YES**
          - Is there a laboratory confirmed Influenza A or B in at least one of the ILI cases?
            - **YES**
            - Initiate oseltamivir prophylaxis for all residents in the affected area(s) immediately
          - **NO**
          - Continue with outbreak management excluding prophylaxis

  - **YES**
    - Do PCR results confirm Influenza?
      - **YES**
      - Is the pathogen confirmed less than 1 day after the outbreak was declared?
        - **YES**
        - Initiate oseltamivir prophylaxis for all residents in the affected area(s) immediately
        - **NO**
        - Continue with outbreak management excluding prophylaxis
      - **NO**
      - Continue with outbreak management excluding prophylaxis

- **YES**
  - Presence of considerations that lower the threshold for prophylaxis?
    - **YES**
    - Consider initiating oseltamivir prophylaxis for all residents in the affected area(s)
    - **NO**
    - Initiate oseltamivir prophylaxis for all residents in the affected area(s) immediately

Presence of considerations that lower the threshold for prophylaxis:
- Confirmed pathogen is influenza A
- Daily increasing cases and outbreak curve is on the rise
- High attack rate
- Severe disease and/or observations of mortality or hospitalizations
- Cohorting of ill residents and staff not feasible
- Low vaccination rates and/or poor vaccine strain match

Presence of considerations that do not lower the threshold for prophylaxis:
- Confirmed pathogen is influenza B
- The outbreak curve is at its peak or trending down and/or new cases have not occurred for approximately 4 days
- Low attack rate
- Mild disease and no attributable mortality or hospitalizations
- Residents are capable of complying with Droplet Contact precautions (including isolation to the room) and/or cohorting of ill residents is feasible
- Staff are cohorted (e.g., working on the same unit for the outbreak duration)

Medical Director to discuss plan with Dr. Bunmi Fayote (204-940-3605) or Medical Officer of Health on-call (204-788-8666)

Rapid tests are negative and PCR test results are pending

PCR results return within 24 hours

Do PCR results confirm Influenza?

Is there presence of considerations that lower the threshold for prophylaxis?

Consider initiating oseltamivir prophylaxis for all residents in the affected area(s)