NWT GUIDELINES FOR THE USE OF OSELTAMIVIR IN LONG TERM CARE FACILITIES

Purpose

To provide guidance to infection control professionals, clinicians, and directors of long-term care (LTC) facilities in the Northwest Territories on the use of oseltamivir for treatment and prophylaxis of influenza during an outbreak. **Routine use of antiviral prophylaxis of asymptomatic contacts outside an institutional outbreak is not recommended.** Any resident who is placed on antiviral **prophylaxis** should be carefully monitored for the development of influenza-like (ILI) symptoms. If ILI symptoms develop during prophylaxis, the client should immediately be switched to antiviral **treatment** protocol so as not to create antiviral drug resistance.

An outbreak of influenza is defined as:

- Two or more cases of flu-like illness occur in the same area within 7 days* **AND**
- At least one case is lab-confirmed as influenza.

Any outbreak/suspected outbreak of influenza or influenza-like illness **MUST** be reported to the Office of the Chief Public Health Officer (OCPHO) by phone (867) 920-8646. Only the CPHO (or delegate) can declare an outbreak.

***Timeframe:** Symptoms appear within a 7-day period (often tightened to 48 hours in specific institutional units).

Health Care Professionals:

For **Part 2** written report within 24 hours

- Confirmed case:
  - **Immediately** report all deaths of a patient diagnosed with influenza, whether influenza was the cause of death or a contributing factor, MUST be reported to the OCPHO via the OCPHO Reporting Line (867)920-8646
- Outbreak or suspected outbreak
  - **Immediately** report all outbreaks of confirmed influenza or influenza-like illness by telephone (867)-920-8646 to the OCPHO and if in a facility follow the Reporting of Long-Term Care Facility Outbreaks algorithm and Guidelines on the use of oseltamivir in long-term care facilities
- Laboratories
  - Report all positive results to the OCPHO by fax (867) 873-0442 within **24 hours**

It is recommended to monitor the seasonal influenza surveillance reports for strain circulation, vaccine-strain match and antiviral resistance and remain up to date on OCPHO alerts.

- Canada (FluWatch)
- NWT Wastewater monitoring: https://www.hss.gov.nt.ca/en/services/wastewater-monitoring/wastewater-trends
- CPHO Practitioner Alerts: https://ournthssa.ca/post_category/cpho-practitioner-alerts/

Early initiation of antiviral treatment for symptomatic eligible residents is critical for effective treatment

- The most responsible health care practitioner (MRP) is accountable to determine eligibility and prescribe treatment.
- Refer to Association of Medical Microbiology and Infectious Disease (AMMI) Canada guidance for identification of suspect influenza cases and indications for early antiviral treatment.

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 LTC facility should populate a spreadsheet (contact line list) with the resident demographic information and 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 Infectious Diseases	

Antiviral Treatment for Influenza or Influenza-like symptoms:

- Initiate oseltamivir treatment **immediately** for LTC residents with signs and symptoms of ILI.
- Influenza-Like-Illness (ILI) Definition:
  - Acute onset of respiratory illness which includes cough (new or worsening chronic cough) and one or more of the following symptoms:
    - Fever
    - Shortness of breath
    - Sore throat
    - Myalgia
    - Arthralgia
    - Prostration

    NOTE: In adults 65 years of age and older fever may not be prominent.
- 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 consideration of extended treatment may be extended for severely ill individuals in consultation with the most responsible physician (MRP).
- **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 an Infectious Disease expert.

Antiviral Prophylaxis for Influenza or Influenza-like symptoms:

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 NWT Communicable Disease Control Manual chapter on Influenza, Alberta's Guide For Outbreak Prevention and Control in Continuing Care Homes and NTHSSA Influenza Outbreak Control Measures Guidance Appendix B
- Ensure confirmed or suspected outbreak is reported to OCPHO and to relevant HSSA departments (IPAC, Continuing Care) and consult the CPHO regarding approval for oseltamivir prophylaxis. Only the CPHO (or delegate) can declare an outbreak.

- 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 symptoms.
- Careful daily review of any resident on prophylaxis for onset of any ILI symptoms IS REQUIRED so that resistance to oseltamivir is not created
- Due to the incubation and transmission periods, it is expected that new cases of influenza will continue to occur for up to 5 days after prophylaxis has been started. However, it is unusual to see new cases more than five full days after prophylaxis has been started. Consequently, antiviral prophylaxis can be stopped on Day 10 or when the outbreak can be declared over whatever is shorter.
    - This guidance does not address antiviral prophylaxis for health care staff, time off work during an influenza outbreak for unvaccinated or high-risk staff nor vaccination policies for healthcare workers in long term care facilities. Please refer to your occupational health staff or policies for further guidance.
    - If the outbreak is not over after 10 days (no new ILI cases, the MRP should consult with the Chief Public Health Officer to determine if oseltamivir prophylaxis should continue.

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

- **Oseltamivir is a MUST STOCK item as per the NWT Primary Care Formulary**
    - 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**

References

Alberta public health disease management guidelines: influenza, seasonal. https://open.alberta.ca/publications/influenza

Alberta Guide for Outbreak Prevention and Control in Continuing Care Homes. https://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-ob-guide-for-outbreak-prevention-and-control-in-continuing-care-homes.pdf

AMMI Guidelines. Aoki, F.Y., Allen, U.D., Mubareka, S., Papenburg, J., Stiver, H.G., & Evans, G.A. (2019). Use of antiviral drugs for seasonal influenza: Foundation document for practitioners—Update 2019. *Journal of the Association of Medical Microbiology and Infectious Disease Canada, 4* (2), 60-82. doi:10.3138/jammi.2019.02.08 https://ammi.ca/en/resources/

Buckrell S, Ben Moussa M, Bui T, Rahal A, Schmidt K, Lee L, Bastien N, Bancej C. (2022). National Influenza Annual Report, Canada, 2021–2022: A brief, late influenza epidemic. *Can Commun Dis Rep, 48*(10):473−83. https://doi.org/10.14745/ccdr.v48i10a07

NTHSSA Influenza Outbreak Control Measures. https://ournthssa.ca/wp-content/uploads/2022/11/Appendix-B-Influenza-Outbreak-Control-Measures.pdf

NTHSSA Outbreak Management. https://ournthssa.ca/wp-content/uploads/2022/10/12-54-V1-Outbreak-Management-002.pdf

NWT Communicable Disease Manual. https://www.hss.gov.nt.ca/professionals/en/services/nwt-communicable-disease-manual

NWT Long Term Care Standards. https://www.hss.gov.nt.ca/professionals/sites/professionals/files/resources/nwt-ltc-standards.pdf

NWT Primary Care Formulary. https://www.hss.gov.nt.ca/professionals/sites/professionals/files/resources/nwt-primary-care-forumulary.pdf

Public Health Agency of Canada (PHAC). FluWatch https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance.html

Uyeki, T. M., Bernstein, H. H., Bradley, J. S., Englund, J. A., File Jr, T. M., Fry, A. M., ... & Pavia, A. T. (2019). Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clinical Infectious Diseases, 68*(6), e1-e47. doi: 10.1093/cid/ciy874