

Northern Inter-Tribal Health Authority

Use of Antiretroviral Medication – Oseltamivir (Tamiflu) for Prevention and Treatment of Seasonal Influenza

RN Specialty Practice Guide

Updated October 26, 2022





Use of antiretroviral medication - Oseltamivir (Tamiflu) for prevention and treatment of seasonal influenza

Practice guide for RN (AAPs) & Nurse Practitioners

Purpose

The purpose of this document is to provide RN (AAPs), Nurse Practitioners and Physicians with information on the use of antiviral drug - **OSELTAMIVIR PHOSPHATE** (Tamiflu) for the treatment of seasonal influenza in northern First Nations communities.

Tamiflu is effective in reducing the length and complications of symptoms following the infection of influenza.

This guideline applies to patients who have symptoms suggestive of Influenza according to the WHO case definition (Acute respiratory illness with measured temperature $\geq 38^{\circ}\text{C}$ and cough).

Use of Tamiflu within the provision of this guideline is restricted to peak influenza season, typically between October and April.

Laboratory confirmation of influenza during peak flu season is not necessarily required for initiation of antiviral treatment, nor should treatment be delayed while waiting for laboratory results from external lab services. The use of the Genex machines is also available in some NITHA communities for the detection of Influenza A and B Viruses.

Clinical use is based on the duration and severity of symptoms, client risk and recent influenza vaccine history.

OSELTAMIVIR PHOSPHATE (Tamiflu®):

Oseltamivir is a drug which prevents the spread of the influenza virus in an infected person. It is a neuraminidase inhibitor which inhibits the enzyme responsible for cleaving the viral load from the host cell thus preventing it from further dissemination. It is active against both influenza A and B viruses.

Indications and Recommendations:

Oseltamivir is indicated for the treatment of influenza in patients 1 year of age and older within 2 days (48 hours) of onset of symptoms of influenza-like illness (ILI). The efficacy for Oseltamivir has not been established for those patients beginning treatment after this 2-day period but may be considered at clinician discretion.

Oseltamivir is prescribed as an adjunct to influenza vaccination but is not a substitute for the vaccine. Oseltamivir is not approved in Canada for children younger than 1 year of age. Oseltamivir use for seasonal influenza in children younger than 1 year of age should be considered on a case-by-case basis, with focus on severity of illness. Consultation with a pediatrician would be beneficial.



Where influenza is reasonably suspected on clinical grounds, antiviral treatment of high-risk individuals should not await the diagnostic test result and should be initiated as soon as possible, ideally within 48 hours of ILI onset, irrespective of influenza vaccination status.

Clinicians may consider personalized plans for timely antiviral drug access and use for patients at highest risk of serious influenza complications (in particular, elderly adults and people of any age with cardio-pulmonary conditions or severe immunodeficiency states).

Contraindications:

Any client that with a history of anaphylaxis or severe reaction to the Oseltamivir (Tamiflu).

Hypersensitivity to the drug or any of its excipients. The drug formulation contains pregelatinized starch, talc, povidone K 30, croscarmellose sodium, and sodium stearyl fumarate. The capsule shell contains a gelatin, titanium dioxide, yellow iron oxide, black iron oxide, red iron oxide and FD&C Blue No. 2 colorant.

Persons with severe kidney disease are contraindicated.

Pharmacokinetics:

Oseltamivir is administered orally. Oseltamivir is a prodrug that is hepatically metabolized extensively to Oseltamivir carboxylate by hepatic esterases. Oseltamivir and Oseltamivir carboxylate have low protein binding. Neither Oseltamivir nor Oseltamivir carboxylate are substrates, nor inhibitors of the cytochrome P450 isoenzymes.

Oseltamivir carboxylate is eliminated renally by excretion into the urine. Dosage adjustments are recommended inpatients with renal impairment and with serum creatinine clearance < 30 mL/min.

Precautions:

Safety in hepatic impairment has not been established. Adjust dosing if serum creatinine < 30mL/min. Pregnancy category C: crosses the placenta and secreted into breast milk but no human data safety; use in pregnancy and lactation only if potential benefits outweigh the risks. Pregnant or breastfeeding women should not be administered the Oseltamivir (Tamiflu). Consultation with an obstetrician should be considered with severe cases.

Drug Interactions:

No significant drug interactions. Co-administration with probenecid may result in a 2-fold increase in exposure to Oseltamivir carboxylate, however this does not compromise the safety margin of the oseltamivir carboxylate.

Adverse Effects:

Nausea and vomiting are reported most commonly and are generally mild to moderate, occurring during the first 2 days of therapy.

Other less common effects include diarrhea, abdominal pain, otitis media/ear disorder, asthma, epistaxis, pneumonia, sinusitis, bronchitis, conjunctivitis, dermatitis, lymphadenopathy and tympanic membrane disorder.



Observed effects ([post-marketing]): rash, swelling of the face or tongue, toxic epidermal necrolysis, dermatitis, rash, eczema, urticaria, erythema multiforme, Stevens-Johnson-Syndrome, hepatitis, abnormal liver function tests, arrhythmia, seizure, confusion, anaphylactic reactions, and aggravation of diabetes. The causal relationship of these adverse effects to the drug has not been established.

Table 1: Risk factors for development of severe influenza

- 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 congestive heart failure and symptomatic coronary artery disease)
- Malignancy
- Chronic renal insufficiency
- Diabetes mellitus and other metabolic diseases
- Hemoglobinopathies such as sickle cell disease
- Immunosuppression or immunodeficiency due to disease (e.g. HIV infection, especially if CD₄ is <200x10⁶/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)
- Children younger than 5 years of age*
- Individuals 65 years of age or 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
- Individuals <18 years of age who are on chronic aspirin therapy
- Obesity with a BMI ≥40 or a BMI <3 z-scores above the mean for age and gender
- Indigenous peoples
- Persons who are living in shelters, homeless or overcrowding

*Children who are two through four years of age also have a higher rate of complications compared to older children; however, the risk for these children is lower than the risk for children younger than two years of age.



Other Information:

Store Oseltamivir medication at room temperature.

This drug is covered under the NIHBU.

Health clients with relatively mild influenza are not likely to benefit from antiviral therapy initiated over 48 hours of onset.



References

Aoki FY, Allen UD, Mubareka S, Papenburg J, Stiver HG, Evans GA. Use of antiviral drugs for seasonal influenza: Foundation document for practitioners—Update 2019. *Official Journal of the Association of Medical Microbiology and Infectious Disease Canada*. 2019 Jun;4(2):60-82.

Blanton L, Peacock G, Cox C, et al. 2012. Neurologic disorders among pediatric deaths associated with the 2009 pandemic influenza. *Pediatrics*; 130:390-6.

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<https://www.ammi.ca/Content/Guidelines/Flu%20%28published%20version%29%20FINAL.pdf>

National Advisory Committee on Immunization (NACI) Canadian Immunization Guide. Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022-23.

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<https://www.ehealthsask.ca/services/Manuals/Pages/default.aspx>

Upton D. Allen 2018. Canadian Paediatric Society, The use of antiviral drugs for influenza: Guidance for practitioners <https://www.cps.ca/en/documents/position/antiviral-drugs-for-influenza>

World Health Organization 2018: Revision of clinical case definitions: influenza-like illness and severe acute respiratory infection *Bulletin of the World Health Organization* Volume 96, Number 2, February 2018, 77-144 <https://www.who.int/bulletin/volumes/96/2/17-194514/en/>



Decision Aid Algorithm for Influenza Testing

Does patient have symptoms suggestive of influenza according to the WHO case definition (Acute respiratory illness with measured temperature $\geq 38^{\circ}\text{C}$ and cough, with onset within past 10 days¹)?

YES

NO

Is the patient:

- Being admitted to hospital??
- OR - Part of an outbreak investigation?
- OR - In a risk category for developing influenza-related complications?²
 - Age <5 or >65
 - Pregnant or <4 wks post-partum
 - Immunocompromised
 - Indigenous
 - Chronic health conditions

Influenza testing NOT indicated

- Not likely to be Influenza Type A
- Look for other etiology

YES

NO

Will influenza test results influence clinical management?^{**}

Submit nasopharyngeal swab for Influenza testing

YES

NO

Probable Influenza Type A based on clinical presentation

- No laboratory testing required
- Monitor and manage accordingly

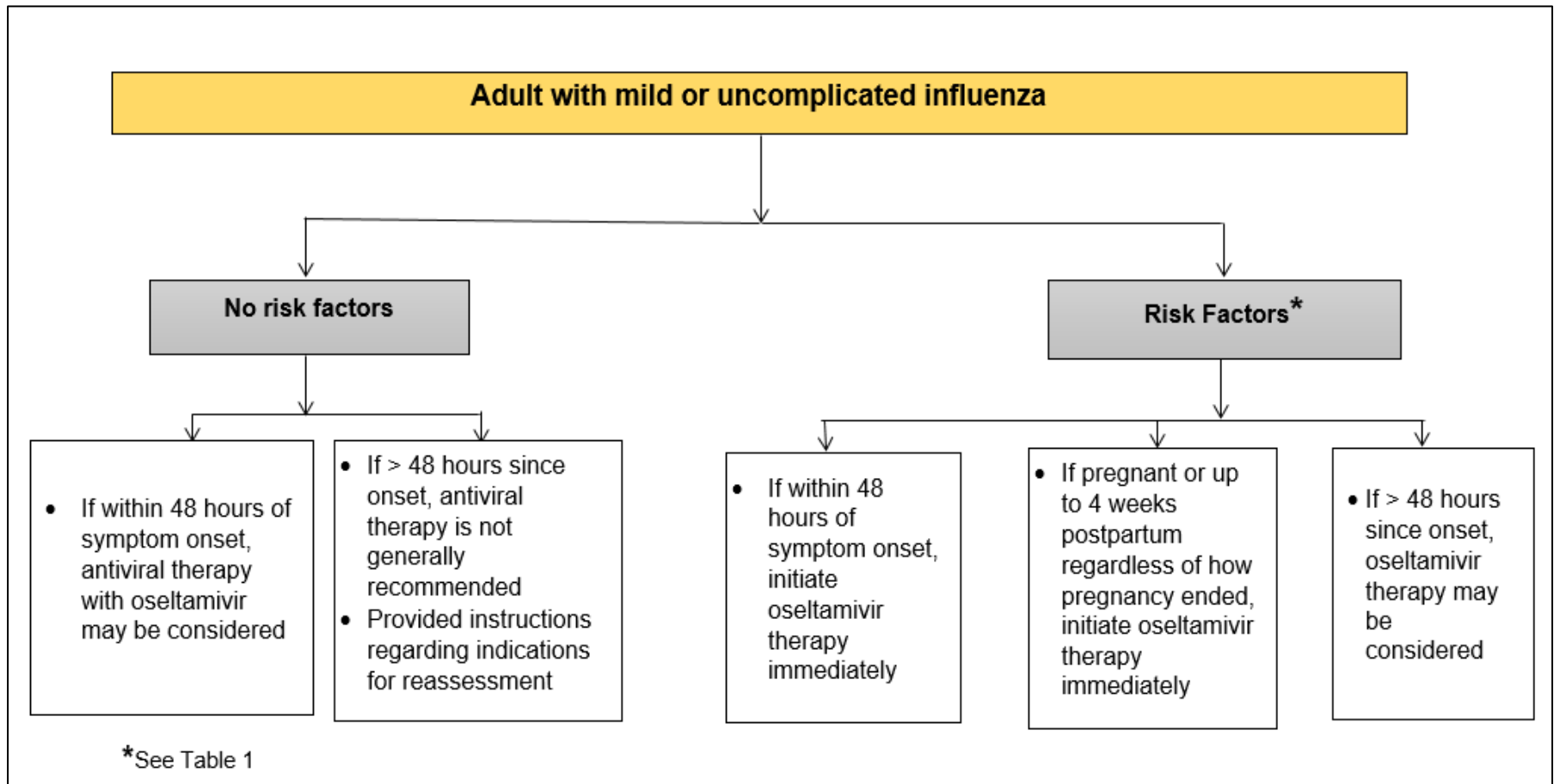
^{**}Please note: Laboratory confirmation of influenza during peak flu season is not needed for initiation of antiviral treatment, nor should treatment be delayed while waiting for laboratory results

^{**}Please note: Infection control precautions are indicated for all patients with signs and symptoms suggestive of a viral respiratory infection. Implementing precautions does not depend upon laboratory results, and should not be delayed while waiting for laboratory results

Adapted from Roy Romanow Provincial Laboratory October 2019



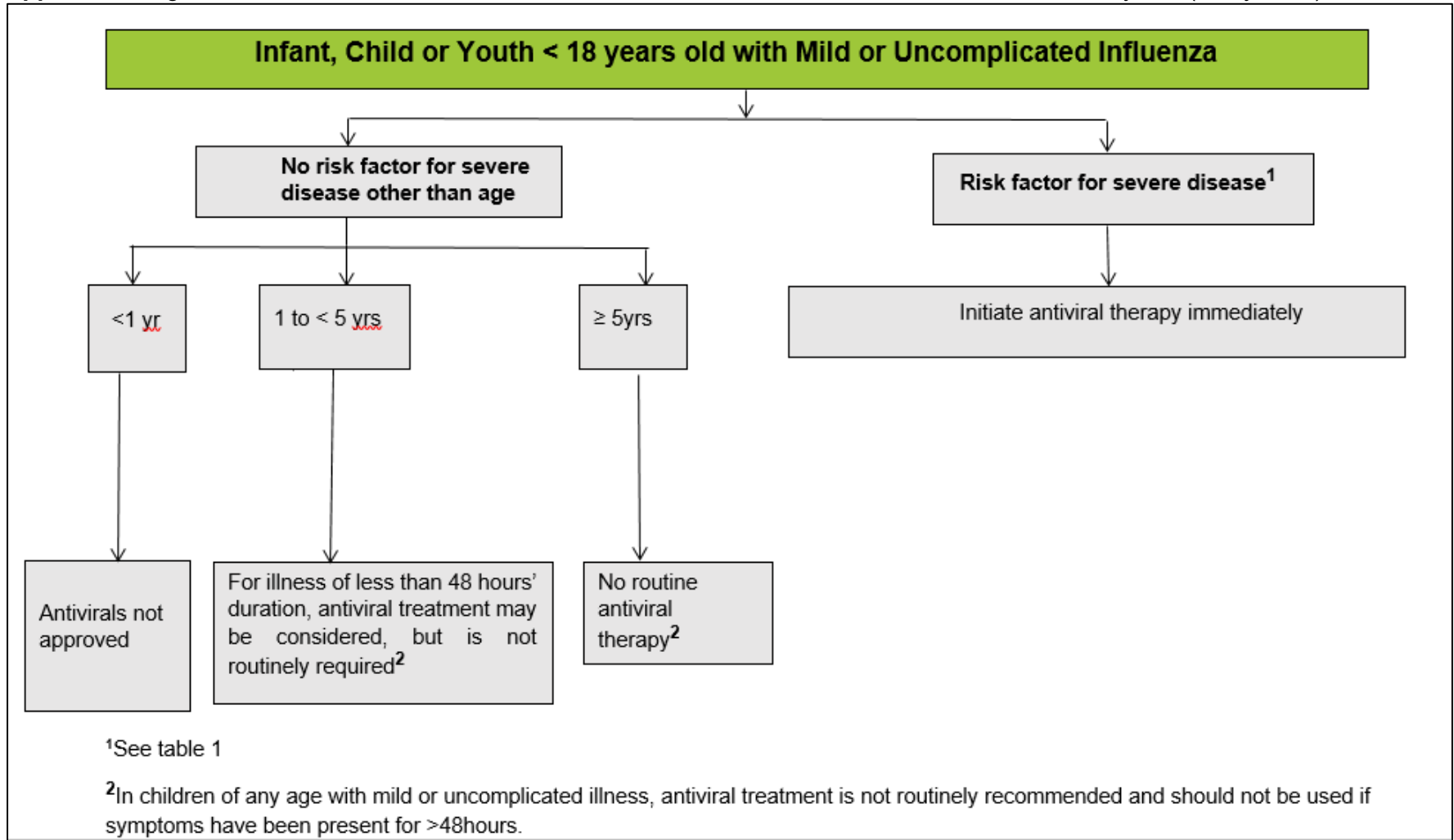
Appendix B Algorithm for oseltamivir treatment of MILD or UNCOMPLICATED influenza in adults



Adapted from Aoki FY et al, AMMI 2019



Appendix C Algorithm for oseltamivir treatment of **MILD** or **UNCOMPLICATED** influenza in children and youth (<18 yrs old)



Adapted from Aoki FY et al, AMMI 2019



Appendix D Oseltamivir treatment of seasonal influenza (treatment regimens)

Body Weight, Age or Serum Creatinine		Treatment for 5 Days	Chemoprophylaxis for 10 Days
Body weight			
Body weight (kg)	Body weight (lbs)		
≤15 kg	≤33 lbs	30 mg twice daily	30 mg once daily
>15 kg to 23 kg	>33 lbs to 51 lbs	45 mg twice daily	45 mg once daily
>23 kg to 40 kg	>51 lbs to 88 lbs	60 mg twice daily	60 mg once daily
>40 kg	>88 lbs	75 mg twice daily	75 mg once daily
Age			
≥13 years and older		75 mg twice daily	75 mg once daily
Serum Creatinine clearance			
>60 mL/min		75 mg twice daily	75 mg once daily
30 to 60 mL/min		75 mg once daily	30 mg once daily
10 to 30 mL/min		30 mg once daily	30 mg on alternate days
<10 ml/min (renal failure)		Single 75 mg dose for the duration of illness	NA