Algorithm for oseltamivir and zanamivir treatment of mild or uncomplicated influenza in adults.

Adapted from: *The Use of Antiviral Drugs for Influenza: A Foundation Document for Practitioners*
Published in the Canadian Journal of Infectious Diseases and Medical Microbiology 2013;24(Suppl C):1C-15C

### Adult with mild or uncomplicated influenza

**No risk factors**
- If within 48 hours of symptom onset, antiviral therapy with oseltamivir or inhaled zanamivir may be considered
- If > 48 hours since onset, antiviral therapy is not generally recommended
- Provide instructions regarding indications for reassessment

**Risk factors**
- If within 48 hours of symptom onset, initiate oseltamivir or inhaled zanamivir therapy immediately
- If pregnant or up to 4 weeks postpartum regardless of how pregnancy ended, initiate oseltamivir or inhaled zanamivir therapy immediately
- If > 48 hours since onset, oseltamivir or zanamivir therapy may be considered

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1 Adult relevant risk factors:
- 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 <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 or older
- People of any age who are residents of nursing homes of other chronic care facilities
- Pregnant women and women up to 4 weeks postpartum regardless of how pregnancy ended
- Obesity with a BMI≥ 40 or a BMI >3 z-scores above the mean for age and gender
- Aboriginal Peoples
Appendix B  Algorithm for oseltamivir and zanamivir treatment of moderate, progressive, severe or complicated influenza in adults.

Adapted from: The Use of Antiviral Drugs for Influenza: A Foundation Document for Practitioners
Published in the Canadian Journal of Infectious Diseases and Medical Microbiology 2013;24(Suppl C):1C-15C

Adult with moderate, progressive, severe or complicated illness

- Consider hospitalization
- Consider admission to intensive care unit

Initiate antiviral therapy immediately even if the interval between symptom onset and initiation of therapy is longer than 48 hours

- Those not responding to oseltamivir therapy
- Those with illness despite oseltamivir prophylaxis
- Where influenza B is confirmed or strongly suspected

Others

- Oseltamivir
  75 mg BID for 5-10 days

Not responding

Zanamivir
Intravenous zanamivir, if available*, is preferred to inhaled zanamivir
(*through clinical trials or via Health Canada’s Special Access Program)

Test for oseltamivir resistance
Algorithm for oseltamivir and zanamivir treatment of influenza in children and youth (<18 yrs. old)

Adapted from: The Use of Antiviral Drugs for Influenza: A Foundation Document for Practitioners
Published in the Canadian Journal of Infectious Diseases and Medical Microbiology 2013;24(Suppl C):1C-15C

Infant, child or youth <18 yrs old with influenza

Mild or uncomplicated illness

Moderate, progressive, severe or complicated influenza

No risk factors for severe disease other than age

Risk factors for severe disease¹

Consider hospitalization including ICU admission²

Risk factors for severe disease¹

Initiate antiviral therapy immediately

No previous oseltamivir exposure

No routine antiviral therapy³

For illness of less than 48 hours’ duration, antiviral treatment may be considered, but is not routinely required³

1. Zanamivir (IV zanamivir⁴ is recommended if the inhalation device cannot be used)

2. Test for oseltamivir resistance

Oseltamivir therapy

Antivirals not approved; use on a case-by-case basis³

¹ Pediatric relevant risk factors:
- 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)
- Malignancy
- Chronic renal insufficiency
- Diabetes mellitus and other metabolic diseases

- Hemoglobinopathies such as sickle cell disease
- Immunosuppression or immunodeficiency due to disease, 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
- Residents of chronic care facilities

² Treatment with oseltamivir or, if appropriate zanamivir may be considered on a case-by-case basis even if symptoms have been present for >48 h. In Canada, antivirals are not authorized for infants < 1 year of age but should be considered

³ In children of any age with mild or uncomplicated illness, antiviral treatment is not routinely recommended and should not be used if symptoms have been present for >48 h

⁴ Accessed through available clinical trials or via Health Canada’s Special Access program

* 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.

* Pregnant adolescents and adolescents up to 4 weeks post partum regardless of how the pregnancy ended (see Appendix A)
- Individuals <18 years of age who are on chronic aspirin therapy
- Obesity with a BMI > or a BMI >3 z-scores above the mean for age and gender
- Aboriginal Peoples
Appendix D  Algorithm for oseltamivir and zanamivir prophylaxis or early treatment in close contacts of suspected or lab-confirmed case.

Adapted from: The Use of Antiviral Drugs for Influenza: A Foundation Document for Practitioners
Published in the Canadian Journal of Infectious Diseases and Medical Microbiology 2013;24(Suppl C):1C-15C

<table>
<thead>
<tr>
<th>Close contact of case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resident of closed facility</td>
</tr>
<tr>
<td>Others</td>
</tr>
</tbody>
</table>

- **Resident of closed facility**
  - No risk factors for influenza complications especially if influenza immunization is up to date
  - Not immunosuppressed
  - Early treatment with oseltamivir if symptoms arise

- **Others**
  - Risk factors for influenza complications
    - Significant Immunosuppression
    - Presumptive treatment
      - with oseltamivir or zanamivir

† Presumptive treatment is therapy with twice daily doses of oseltamivir or zanamivir initiated before the onset of influenza symptoms in close contacts of individual with suspected or lab-confirmed influenza illness.

1 Risk factors for influenza complications 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 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 <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)
- Children younger than 5 years of age
- People of any age who are residents of nursing homes of 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
- Aboriginal Peoples

* 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.
### Oseltamivir and zanamivir treatment of influenza (treatment regimens)

Adapted from: *The Use of Antiviral Drugs for Influenza: A Foundation Document for Practitioners*

*Published in the Canadian Journal of Infectious Diseases and Medical Microbiology 2013;24(Suppl C):1C-15C*

#### Medication Treatment (5 days) | Chemoprophylaxis (10 days)
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**Oseltamivir**
**Adults** | 75 mg twice daily | 75 mg once daily
**Children ≥ 12 months**
<table>
<thead>
<tr>
<th>Body Weight (kg)</th>
<th>Body Weight (lbs)</th>
<th>Body Weight (kg)</th>
<th>Body Weight (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤15 kg</td>
<td>≤33 lbs</td>
<td>30 mg twice daily</td>
<td>30 mg once daily</td>
</tr>
<tr>
<td>&gt; 15 kg to 23 kg</td>
<td>&gt; 33 lbs to 51 lbs</td>
<td>45 mg twice daily</td>
<td>45 mg once daily</td>
</tr>
<tr>
<td>&gt;23 kg to 40 kg</td>
<td>&gt; 51 lbs to 88 lbs</td>
<td>60 mg twice daily</td>
<td>60 mg once daily</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>&gt; 88 lbs</td>
<td>75 mg twice daily</td>
<td>75 mg once daily</td>
</tr>
</tbody>
</table>
**Children 3 months to < 12 months**
| 3 mg/kg/dose twice daily | 3 mg/kg/dose once per day |
**Children < 3 months**
| 3 mg/kg/dose twice daily | Not recommended unless situation judged critical due to limited data on use in this age group |

*Please note that antivirals are not authorized in Canada for the routine treatment of seasonal influenza illness in infants less than 1 year of age. Such use may be considered on a case-by-case basis.*

#### Zanamivir
**Adults**

| 10 mg (two 5 mg inhalations) twice daily | 10 mg (two 5 mg inhalations) once daily |

**Children (≥7 years or older for treatment and chemoprophylaxis)**

| 10 mg (two 5 mg inhalations) twice daily | 10 mg (two 5 mg inhalations) once daily |

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1. Oseltamivir is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available in 30 mg, 45 mg, and 75 mg capsules, and as a powder for oral suspension that is reconstituted to provide a final concentration of either 6 mg/mL or 12 mg/mL. If the commercially manufactured oral suspension is not available, the capsules may be opened and the contents mixed with a sweetened liquid to mask the bitter taste or a suspension can be compounded by retail pharmacies.

When dispensing commercially manufactured Oseltamivir (TAMIFLU) Powder for Oral Suspension (6 mg/mL or 12 mg/mL), pharmacists should ensure the units of measure on the prescription instructions match the dosing device.

2. Weight-based dosing is preferred. Give two doses per day for treatment and one dose per day for prophylaxis. However, if weight is not known, dosing by age in full-term infants younger than 1 year of age may be necessary: 0-3 months = 12 mg per dose for treatment, but prophylaxis is not recommended; 3-5 months 20 mg per dose; 6-11 months = 25 mg per dose.

3. Current weight-based dosing recommendations are not intended for premature infants. Premature infants may have slower clearance of oseltamivir due to immature renal function, and doses recommended for full term infants may lead to very high drug concentrations in this age group. Very limited data from a cohort of premature infants demonstrated that oseltamivir concentrations among premature infants given 1 mg/kg body weight twice daily were similar to those observed with the recommended treatment doses in term infants (3 mg/kg body weight twice daily). Observed drug concentrations were highly variable among premature infants. The IDSA 2011 recommendations for pediatric pneumonia suggest 2 mg/kg/day divided twice daily. Currently available data are insufficient to recommend a specific dose of oseltamivir for premature infants; it is strongly suggested that an infectious disease physician or clinical pharmacist should be consulted.

4. Zanamivir is administered by inhalation using a proprietary "Diskhaler" device distributed together with the medication. Zanamivir is a dry powder, not an aerosol, and should not be administered using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for persons with chronic respiratory diseases such as asthma or chronic obstructive pulmonary disease that increase the risk of bronchospasm.